STIC 1

Lucas, Z
10/698086

FILE 'CAPLUS' ENTERED AT 15:21:16 ON 11 FEB 2005

L18 1998 SEA FILE=CAPLUS ABB=ON PLU=ON (ADENOVIR? OR ADENO VIR?)(W)EAR LY OR EARLY(W)PROTEIN

L19 1603 SEA FILE=CAPLUS ABB=ON PLU=ON L18 AND (VIRUS? OR VIRAL? OR HERPES? OR (HSV OR HV)(S)HERPES?)

L20 80 SEA FILE=CAPLUS ABB=ON PLU=ON L19 AND (RENAL? OR KIDNEY OR RETINA# OR AMNIOT? OR EYE OR OCULAR OR OPTIC?)

L21 44 SEA FILE=CAPLUS ABB=ON PLU=ON L20 AND (DNA OR DEOXYRIBONUCLEI C OR DEOXY RIBONUCLEIC OR NUCLEIC)

L22 20 SEA FILE=CAPLUS ABB=ON PLU=ON L21 AND (DETERM? OR DETECT? OR DET## OR SCREEN?)

L22 ANSWER 1 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 11 Mar 2003

ACCESSION NUMBER: 2003:187420 CAPLUS

DOCUMENT NUMBER: 138:332803

TITLE: **Detection** of human cytomegalovirus **DNA** replication in non-permissive vero and 293 cells

AUTHOR(S): Ellsmore, Victoria; Reid, G. Gordon; Stow, Nigel D.

CORPORATE SOURCE: MRC Virology Unit, Institute of Virology, Glasgow, G11 5JR, UK

SOURCE: Journal of General Virology (2003), 84(3), 639-645
CODEN: JGVIAY; ISSN: 0022-1317

PUBLISHER: Society for General Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Human cytomegalovirus (HCMV) displays an exceptionally restricted host range in tissue culture with human fibroblasts being the principal fully permissive system. Nevertheless, immediate early (IE) proteins are expressed following infection of many non-permissive cell types of human, simian and murine origin, and **viral** origin-dependent **DNA** synthesis has been reconstituted by transfection of plasmids into Vero cells, a non-permissive line from African green monkey. We have examined the accumulation of HCMV strain AD169 **DNA**, and the replication of transfected HCMV origin-containing plasmids, in infected Vero and human embryonic **kidney** 293 cells, which were previously reported to express the major IE protein in a small proportion of infected cells but to be non-permissive for **viral DNA** synthesis. In Vero cells accumulation of origin-containing plasmid but not **viral DNA** occurred, while in 293 cells both **DNAs** accumulated. Immunofluorescence expts. indicated that following infection with 3 p.f.u. per cell, a small fraction of both cell types expressed the UL44 **DNA** replication protein. Neither cell line, however, supported the generation of infectious progeny **virus**. These results suggest that IE proteins expressed in Vero and 293 cells can induce the synthesis of **early proteins** capable of functioning in **viral DNA** replication, but there is a failure in later events on the pathway to infectious **virus** production This provides further support for transfected Vero cells being a valid system in which to study HCMV **DNA** synthesis, and suggests that 293 cells may also prove useful in similar expts.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 2 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 10 Jan 2003
ACCESSION NUMBER: 2003:23420 CAPLUS
DOCUMENT NUMBER: 138:84582
TITLE: Use of polymorphisms in ORL1 gene encoding orphanin FQ/nociceptin receptor in diagnosis and treatment of diseases
INVENTOR(S): Kreek, Mary Jeanne; Laforge, Karl Steven
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 29 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2003008289	A1	20030109	US 2001-905186		20011009
PRIORITY APPLN. INFO.:			US 2000-218205P	P	20000714

AB The present invention provides single nucleotide polymorphic alleles of human gene encoding orphanin FQ/nociceptin receptor and their use in diagnosis and therapy of dieases. Cloning vectors for replicating such variant alleles, and expressing vectors for expressing the variant alleles to produce variant orphanin FQ/nociceptin receptors are also provided. Host cells may include E.coli, Pseudomonas, Bacillus, Streptomyces, yeast, and animal cell lines CHO, R1.1, B-W, L-M, COS1, COS7, BSC1, BSC40, BMT10 and Sf9 cells.

L22 ANSWER 3 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 15 Nov 2002
ACCESSION NUMBER: 2002:869210 CAPLUS
DOCUMENT NUMBER: 137:346139
TITLE: Methods for the identification of antiviral compounds
INVENTOR(S): Brus, Ronald Hendrik Peter; Uytdehaag, Alphonsus Gerardus Cornelis Maria; Schouten, Govert Johan
PATENT ASSIGNEE(S): Crucell Holland B.V., Neth.
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002090982	A1	20021114	WO 2002-NL296	20020506

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1256803 A1 20021113 EP 2001-201657 20010507
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
EP 1388008 A1 20040211 EP 2002-733606 20020506
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
US 2004086850 A1 20040506 US 2003-698086 20031030
PRIORITY APPLN. INFO.: EP 2001-201657 A 20010507
US 2001-289541P P 20010507
WO 2002-NL296 W 20020506

AB Methods are disclosed for the identification of antiviral compds. The invention provides novel methods for **determining** whether a compound influences a phase in the life cycle of a **virus** comprising providing a cell with said compound and with at least a fragment of said **virus** sufficient for performing said phase and **determing** whether said phase is influenced in said cell, said cell comprising a **nucleic** acid encoding an **adenovirus early protein** or a functional part, derivative and/or analog of said **adenovirus early protein**. In another aspect the invention provides the use of a cell, said cell comprising **nucleic** acid encoding an **adenovirus early protein**, for **screening** a library of compds. for the presence of a compound capable of influencing a phase in the life cycle of a **virus** capable of entering said cell. In yet another aspect, the invention provides novel methods for identifying a compound with antiviral activity comprising providing a cell with at least a fragment of a **virus**, said fragment capable of performing a step in the life cycle of said **virus**, providing said cell with a compound and **determining** whether said compound is capable of influencing said step in the life cycle of said **virus**, wherein said cell comprises a **nucleic** acid encoding an **adenovirus early protein** or a functional part, derivative and/or analog of said **adenovirus early protein**.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 4 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 15 Nov 2002
ACCESSION NUMBER: 2002:866739 CAPLUS
DOCUMENT NUMBER: 137:333126
TITLE: Methods for the identification of antiviral compounds
INVENTOR(S): Brus, Ronald Hendrik Peter; Uytdehaag, Alphonsus Gerardus Cornelis Maria; Schouten, Govert Johan
PATENT ASSIGNEE(S): Crucell Holland B.V., Neth.
SOURCE: Eur. Pat. Appl., 44 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1256803	A1	20021113	EP 2001-201657	20010507
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

WO 2002090982 A1 20021114 WO 2002-NL296 20020506
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
EP 1388008 A1 20040211 EP 2002-733606 20020506
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
US 2004086850 A1 20040506 US 2003-698086 20031030
PRIORITY APPLN. INFO.: EP 2001-201657 A 20010507
US 2001-289541P P 20010507
WO 2002-NL296 W 20020506

AB The invention is concerned among other with means and method for **determining** whether a compound influences a phase in the life cycle of a **virus**. The invention utilizes the striking observation that cells comprising a **nucleic** acid encoding an **adenovirus early protein** or a functional part, derivative and/or analog of said **adenovirus early protein** are capable of replicating a wide variety of **viruses** and thus support all the life cycle steps of these **viruses**. Even **viruses** that are difficult to grow on other cells are replicated by such cells. The cells are therefore particularly well suited for the **screening**, selection, isolation or testing of compds. that influence a step in the life cycle of said **virus**. The invention further provides compds. obtainable by a method of the invention.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 5 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 25 Jun 2000
ACCESSION NUMBER: 2000:423178 CAPLUS
DOCUMENT NUMBER: 133:148988
TITLE: Optimized **viral** dose and transient immunosuppression enable **herpes** simplex **virus** ICP0-null mutants to establish wild-type levels of latency in vivo
AUTHOR(S): Halford, William P.; Schaffer, Priscilla A.
CORPORATE SOURCE: Department of Microbiology, University of Pennsylvania School of Medicine, Philadelphia, PA, 19104-6076, USA
SOURCE: Journal of Virology (2000), 74(13), 5957-5967
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The reduced efficiency with which **herpes** simplex **virus** type 1 (**HSV**-1) mutants establish latent infections in vivo has been a fundamental obstacle in efforts to **determine** the roles of individual **viral** genes in **HSV**-1 reactivation. For example, in the absence of the "nonessential" **viral** immediate-**early protein**, ICP0, HSV-1 is severely impaired in its

ability to (i) replicate at the site of inoculation and (ii) establish latency in neurons of the peripheral nervous system. The mouse **ocular** model of HSV latency was used in the present study to **determine** if the conditions of infection can be manipulated such that replication-impaired, ICP0-null mutants establish wild-type levels of latency, as measured by **viral** genome loads in latently infected trigeminal ganglia (TG). To this end, the effects of inoculum size and transient immunosuppression on the levels of acute replication in mouse **eyes** and of **viral DNA** in latently infected TG were examined Following inoculation of mice with 2 + 103, 2 + 104, 2 + 105, or 2 + 106 PFU/**eye**, wild-type **virus** replicated in mouse **eyes** and established latency in TG with similar efficiencies at all four doses. In contrast, increasing the inoculum size of the ICP0-null mutants n212 and 7134 from 2 + 105 to 2 + 106 PFU/**eye** significantly decreased the levels of infectious **virus detected** in the tear films of mice from days 4 to 9 postinfection. In an attempt to establish the biol. basis for this finding, the effect of **viral** dose on the induction of the host proinflammatory response was examined Quant. reverse transcription-PCR demonstrated that increasing the inoculum of 7134 from 2 + 104 to 2 + 106 PFU/**eye** significantly increased the expression of proinflammatory (interleukin 6), cell adhesion (intercellular adhesion mol. 1), and phagocyte-associated (CD11b) genes in mouse **eyes** 24 h postinfection. Furthermore, transient immunosuppression of mice with cyclophosphamide, but not cyclosporin A, significantly enhanced both the levels of acute n212 and 7134 replication in the **eye** and the levels of mutant **viral** genomes present in latently infected TG in a dose-dependent manner. Thus, the results of this study demonstrate that acute replication in the **eye** and the number of ICP0-null mutant genomes in latently infected TG can be increased to wild-type levels for both n212 and 7134 by (i) optimization of inoculum size and (ii) transient immunosuppression with cyclophosphamide.

REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 6 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 03 Jan 2000
ACCESSION NUMBER: 2000:2475 CAPLUS
DOCUMENT NUMBER: 132:106657
TITLE: An early pseudorabies **virus** protein down-regulates porcine MHC class I expression by inhibition of transporter associated with antigen processing (TAP)
AUTHOR(S): Ambagala, Aruna P. N.; Hinkley, Susanne; Srikumaran, Subramaniam
CORPORATE SOURCE: Department of Veterinary and Biomedical Sciences, University of Nebraska, Lincoln, NE, 68583, USA
SOURCE: Journal of Immunology (2000), 164(1), 93-99
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The objectives of this study were to identify the mechanism(s) of pseudorabies **virus** (PrV)-induced down-regulation of porcine class I mols. and the **viral** protein(s) responsible for the

effect. The ability of PrV to interfere with the peptide transport activity of TAP was **determined** by an in vitro transport assay. In this assay, porcine **kidney** (PK-15) cells were permeabilized with streptolysin-O and incubated with a library of 125I-labeled peptides having consensus motifs for glycosylation in the endoplasmic reticulum (ER). The efficiency of transport of peptides from the cytosol into the ER was **determined** by adsorbing the ER-glycosylated peptides onto Con A-coupled Sepharose beads. Dose-dependent inhibition of TAP activity was observed in PrV-infected PK-15 cells. This inhibition, which occurred as early as 2 h post-infection (h.p.i.), reached the maximum level by 6 h.p.i., indicating that TAP inhibition is one of the mechanisms by which PrV down-regulates porcine class I mols. Infection of cells with PrV in the presence of metabolic inhibitors revealed that cycloheximide a protein synthesis inhibitor, but not phosphonoacetic acid a **herpesvirus DNA** synthesis inhibitor, could restore the cell surface expression of class I mols., indicating that late proteins are not responsible for the down-regulation. Infection in the presence of cycloheximide followed by actinomycin-D, which results in accumulation of the immediate-**early protein**, failed to down-regulate class I, indicating that one or more **early proteins** are responsible for the down-regulation of class I mols.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 7 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 06 Oct 1999
ACCESSION NUMBER: 1999:632844 CAPLUS
DOCUMENT NUMBER: 132:19331
TITLE: Infectivity and expression of the early adenovirus proteins are important regulators of wild-type and ΔE1B adenovirus replication in human cells
AUTHOR(S): Steegenga, Wilma T.; Riteco, Nicole; Bos, Johannes L.
CORPORATE SOURCE: Laboratory for Physiological Chemistry and Centre for Biomedical Genetics, Utrecht University, Utrecht, 3508 TA, Neth.
SOURCE: Oncogene (1999), 18(36), 5032-5043
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An adenovirus mutant lacking the expression of the large E1B protein (ΔE1B) has been reported to replicate selectively in cells lacking the expression of functionally wild-type (wt) p53. Based on these results the ΔE1B or ONYX-015 **virus** has been proposed to be an oncolytic **virus** which might be useful to treat p53-deficient tumors. Recently however, contradictory results have been published indicating that p53-dependent cell death is required for productive adenovirus infection. Since there is an urgent need for new methods to treat aggressive, mutant p53-expressing primary tumors and their metastases we carefully examined adenovirus replication in human cells to **determine** whether or not the ΔE1B **virus** can be used for tumor therapy. The results we present here show that not all human tumor cell lines take up adenovirus efficiently. In addition, we observed inhibition of the expression of **adenovirus early proteins** in tumor cells. We present evidence that these two factors rather than

the p53 status of the cell **determine** whether adenovirus infection results in lytic cell death. Furthermore, the results we obtained by infecting a panel of different tumor cell lines show that **viral** spread of the ΔE1B is strongly inhibited in almost all p53-proficient and -deficient cell lines compared to the wt **virus**. We conclude that the efficiency of the ΔE1B **virus** to replicate efficiently in tumor cells is **determined** by the ability to infect cells and to express the early adenovirus proteins rather than the status of p53.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 8 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 16 Apr 1997
ACCESSION NUMBER: 1997:246402 CAPLUS
DOCUMENT NUMBER: 126:314722
TITLE: Human cytomegalovirus IE1 and IE2 proteins are mutagenic and mediate "hit-and-run" oncogenic transformation in cooperation with the adenovirus E1A proteins
AUTHOR(S): Shen, Yuqiao; Zhu, Hua; Shenk, Thomas
CORPORATE SOURCE: Howard Hughes Medical Institute, Department of Molccular Biology, Princeton University, Princeton, NJ, 08544-1014, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1997), 94(7), 3341-3345
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Some epidemiol. studies have suggested a possible link between human cytomegalovirus (HCMV) infection and various malignancies, and HCMV has been shown to transform cultured cells. However, **viral DNA** is not **detected** in most transformants, and the mechanism by which HCMV might contribute to oncogenesis has remained obscure. Here, the authors show that the HCMV immediate early 1 and 2 genes can cooperate with the adenovirus E1A gene to generate transformed foci of primary baby rat **kidney** cells. HCMV gene expression is transient and **viral DNA** is not present in clonal cell lines derived from the transformed foci. The authors find that the HCMV immediate **early proteins** are mutagenic, and the authors propose that HCMV has the potential to contribute to oncogenesis through a "hit-and-run" mechanism, by inducing mutations in cellular genes.

L22 ANSWER 9 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 13 Mar 1997
ACCESSION NUMBER: 1997:171734 CAPLUS
DOCUMENT NUMBER: 126:207891
TITLE: Polymerase chain reaction assays for the **detection** of cytomegalovirus in organ and bone marrow transplant recipients
AUTHOR(S): Evans, Mary Jo; Edwards-Spring, Yadira; Myers, Jean; Wendt, Alice; Povinelli, Deborah; Amsterdam, Daniel; Rittenhouse-Diakun, Kate; Armstrong, Donald; Murray, Brian M.; et al.

CORPORATE SOURCE: Department of Neurology, Roswell Park Division, State University of New York at Buffalo, Buffalo, NY, USA
SOURCE: Immunological Investigations (1997), 26(1&2), 209-229
CODEN: IMINEJ; ISSN: 0882-0139
PUBLISHER: Dekker
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cytomegalovirus (CMV) infection is ubiquitous and results in a wide spectrum of clin. manifestations ranging from asymptomatic infection to severe life threatening disease. Infection in normal children and adults usually causes no symptoms but in the immunocompromised host, CMV may result in severe opportunistic infections with high morbidity and mortality. Historically, **virus detection** was dependent on culture of the **virus** or on a centrifugation culture system referred to as a shell vial assay. The shell vial assay frequently lacked sensitivity and was unable to **detect** infection in its early phase. Also, as with culture assays, the results were affected by antiviral therapy. The CMV antigenemia assay was developed to provide more rapid results and has gained wide usage. This assay is limited to **detection** of the **virus** in white blood cells and is more sensitive than culture or the shell vial assay. Application of the polymerase chain reaction (PCR) to these problems has resulted in the development of assays for CMV which are more sensitive than previously available methods. This method employs liquid hybridization with 32P labeled probes and gel retardation anal. for **detection** of amplified **DNA** specific for each **virus**. A comparison of the **detection** of CMV by an antigenemia assay or the PCR method in the leukocytes of **renal** transplant patients revealed that the PCR assay **detects** cytomegalovirus earlier and more consistently than the antigenemia assay. Finally, the application of a fluorescent dye **detection** system and image anal. of the acrylamide gel with a laser scanner provides addnl. sensitivity to the **detection** of cytomegalovirus, as well as avoiding the use of radioactivity, making the assay more adaptable to the clin. laboratory

L22 ANSWER 10 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 15 Aug 1996
ACCESSION NUMBER: 1996:484301 CAPLUS
DOCUMENT NUMBER: 125:160216
TITLE: Complementation of a vaccinia **virus** host-range K1L gene deletion by the nonhomologous CP77 gene
AUTHOR(S): Ramsey-Ewing, Anna L.; Moss, Bernard
CORPORATE SOURCE: National Institute Allergy and Infectious Dis., National Inst. Health, Bethesda, MD, 20892-0455, USA
SOURCE: Virology (1996), 222(1), 75-86
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We investigated the host-range restriction of a vaccinia **virus** (VV) K1L deletion mutant in rabbit **kidney** RK13 cells and the ability of the nonhomologous cowpox **virus** CP77 gene to overcome this block. **Viral** early mRNAs were made by K1L- VV but **early protein** synthesis was arrested consistent with a translational block. Replication of **viral DNA** did not

occur and neither intermediate nor late mRNAs or proteins were **detected**. These results indicated that host-range restriction occurs earlier in RK13 cells than in Chinese hamster ovary cells (CHO) cells infected with CP77- VV, where the block occurs at translation of intermediate stage mRNA. We confirmed a report that the CP77 gene, which allows VV replication in CHO cells, could replace the K1L gene for plaque formation in RK13 cells. However, the size of the plaques formed by K1L-CP77+ VV was smaller than those formed by K1L+CP77- VV. Single-step growth curves also showed that the CP77 gene could functionally replace the K1L gene, although formation of infectious **virus** was delayed and did not reach the same level as that of K1L+ VV. Most surprisingly, the dramatic shutoff of **viral** and host gene expression was similar in RK13 cells infected with K1L-CP77- VV and K1L-CP77+ VV and little difference was noted for the first 6 h. Subsequently, in cells infected with the K1L-CP77+ VV, **viral early protein** synthesis was spontaneously resurrected and the replication cycle proceeded. Despite the absence of homol., K1L and CP77 gene products appear to be acting in a common **virus**/cell interaction pathway.

L22 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 20 Jun 1996
ACCESSION NUMBER: 1996:358061 CAPLUS
DOCUMENT NUMBER: 125:31820
TITLE: Immunosuppression induces transcription of murine cytomegalovirus glycoprotein H in the **eye** and at non-**ocular** sites
AUTHOR(S): Duan, Y.; Atherton, S. S.
CORPORATE SOURCE: Dep. Cell. Structural Biol., Univ. Texas Health Sci. Cent., San Antonio, TX, USA
SOURCE: Archives of Virology (1996), 141(3-4), 411-423
CODEN: ARVIDF; ISSN: 0304-8608
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In these studies, **DNA** PCR was used to identify sites of murine cytomegalovirus (MCMV) latency after inoculation of **virus** into the supraciliary space of the **eye**. Reverse transcription (RT) PCR for an immediate early gene and a late gene was used to identify putative sites of **virus** reactivation after methylprednisolone (steroid)-induced immunosuppression. Ten weeks after inoculation of 5X102 PFU of MCMV, BALB/c mice were immunosuppressed by i.m. injection of steroid. Control mice were infected but not immunosuppressed. Two weeks after initiation of immunosuppression, mice were sacrificed. **DNA** and RNA extracted from homogenized tissues were amplified for immediate early gene 1 (IE1) and late gene, glycoprotein H (gH), **DNA** and mRNA by PCR and RT-PCR, resp. Replicating **virus** was **detected** in homogenized **ocular** and non-**ocular** tissues by plaque assay. In the latently infected PBS-treated control group, **viral DNA** was **detected** in the inoculated **eye** and in several non-**ocular** tissues; IE1 mRNA was found in most of the **DNA**-pos. tissues, while gH mRNA was amplified only in a few of the MCMV **DNA**-pos. tissues from a single mouse. After immunosuppression, **viral DNA** and IE1 mRNA were **detected** at a higher frequency in various tissues of

steroid-treated mice. GH mRNA was **detected** in a significantly higher number of the inoculated **eyes**, salivary glands and other non-**ocular** tissues of steroid-treated mice. After immunosuppression, low titers of infectious **virus** were recovered from the salivary glands of steroid-treated mice, but infectious **virus** was not recovered from the inoculated **eye** of either steroid-treated or non-immunosuppressed mice. The **DNA** PCR results suggest that after inoculation of 5+102 PFU of MCMV into the supraciliary space of euthymic BALB/c mice, **virus** becomes latent in the inoculated **eye**, salivary gland and other extraocular tissues. The RT-PCR results suggest that latent MCMV can be reactivated in multiple tissues by immunosuppression.

L22 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 02 Sep 1995
ACCESSION NUMBER: 1995:772784 CAPLUS
DOCUMENT NUMBER: 123:162776
TITLE: Vector, **viral** protein, nucleotide sequence coding therefor and method for inhibiting immune recognition
INVENTOR(S): Johnson, David C.; York, Ian A.
PATENT ASSIGNEE(S): Can.
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9515384	A1	19950608	WO 1994-CA657	19941129
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5750398	A	19980512	US 1993-159890	19931130
CA 2177699	AA	19950608	CA 1994-2177699	19941129
AU 9510611	A1	19950619	AU 1995-10611	19941129
AU 690601	B2	19980430		
EP 731839	A1	19960918	EP 1995-901304	19941129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09506252	T2	19970624	JP 1994-515311	19941129
US 5858376	A	19990112	US 1995-476412	19950607
PRIORITY APPLN. INFO.:			US 1993-159890 A	19931130
			WO 1994-CA657 W	19941129

AB This invention relates to the use of **Herpes** Simplex **Virus** (**HSV**) immediate **early protein** ICP47, **nucleic** acid sequences coding for ICP47, and homologous proteins and **nucleic** acid sequences, to inhibit presentation of **viral** and cellular antigens associated with major histocompatibility class I (MHC class I) proteins to CD8+ T lymphocytes; this inhibition effectively increases infective persistence, which can, for example,

improve the utility of **viral** gene therapy vectors. This invention also pertains to a method for the treatment of **herpesvirus** infections, wherein expression and/or activity of the ICP47 protein or its homolog is inhibited in order to increase immune recognition of **herpesvirus**-infected cells and other cells. This invention also pertains to a method for identifying drugs that interfere with the expression or function of ICP47 and its homologs, and which are useful in treating **herpesvirus** infections, and also pertains to the drugs so identified. Furthermore, this invention pertains to methods for the treatment and prevention of autoimmune diseases, tissue and organ transplant rejection, diabetes, multiple sclerosis, arthritis, and tissue damage accompanying **ocular herpesvirus** infections, wherein ICP47 or its homolog, or **nucleic** acids encoding such proteins, are introduced into the cells of a patient. In addition, this invention pertains to vector elements, vectors, polypeptides and polypeptide fragments that can be utilized for the foregoing purposes.

L22 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 26 Jul 1992
ACCESSION NUMBER: 1992:424058 CAPLUS
DOCUMENT NUMBER: 117:24058
TITLE: Phosphorylation of the retinoblastoma protein is modulated in mouse **kidney** cells infected with polyomavirus
AUTHOR(S): Khandjian, Edward W.; Tremblay, Sandra
CORPORATE SOURCE: Fac. Med., Univ. Laval, Quebec, QC, G1L 3L5, Can.
SOURCE: Oncogene (1992), 7(5), 909-17
CODEN: ONCNES; ISSN: 0950-9232
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Lytic infection with polyomavirus, an oncogenic **DNA**-containing **virus**, leads in G0-arrested primary baby mouse **kidney** (BMK) cell cultures to a mitotic host reaction. In the present work, the authors examined the expression of the retinoblastoma gene (RB) and of its product (Rb) in **virus**-infected BMK cells with the aim of correlating its modulation with the sequential activation of cellular processes leading to the induction of S phase by **virus**. In contrast to cell cycle-regulated genes whose expression is induced by **viral** infection, expression of RB is not altered during the transition from G0/G1 to S phase. In BMK cell cultures irreversibly arrested in the G0 phase of the cell cycle, an unphosphorylated species is the only **detectable** form of the RB protein (Rb). Time course anal. showed that in polyoma-infected cells induced to re-enter the S phase of the cell cycle the appearance of the phosphorylated forms of Rb coincided in time with the accumulation of large T antigen and preceded **DNA** synthesis. During the late phase of infection, the majority of Rb was present as phosphorylated forms. Ongoing **DNA** synthesis was not required for the cells to phosphorylate Rb, indicating that this post-translational modification takes place during the activation of the cellular **DNA**-synthesizing apparatus Using hamster anti-polyoma tumor serum, it was observed that the underphosphorylated form of Rb co-precipitated with polyoma large T antigen extracted from infected cells late during infection. Apparently, interactions between **viral early proteins** encoded by **DNA** tumor **viruses** and the product of RB may play a pivotal role in the

mitogenic effect induced by **viral** infection.

L22 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 21 Jul 1989
ACCESSION NUMBER: 1989:420489 CAPLUS
DOCUMENT NUMBER: 111:20489
TITLE: **Nucleic** acid probes, plasmids, diagnostic system, and method for the **detection** of latent human cytomegalovirus in blood products
INVENTOR(S): Nelson, Jay; Oldstone, Michael B. A.; Southern, Peter
PATENT ASSIGNEE(S): Scripps Clinic and Research Foundation, USA
SOURCE: Eur. Pat. Appl., 70 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 271201	A2	19880615	EP 1987-309680	19871102
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AU 8780506	A1	19880519	AU 1987-80506	19871029
DK 8705757	A	19880505	DK 1987-5757	19871103
FI 8704834	A	19880505	FI 1987-4834	19871103
NO 8704573	A	19880505	NO 1987-4573	19871103
PRIORITY APPLN. INFO.:			US 1986-927278 A	19861104

AB Human cytomegalovirus (HCMV)-derived polynucleotide vectors and probes for **detecting** the presence of HCMV in a human cellular body sample are disclosed, as are diagnostic systems and methods for their use. The probes include a polynucleotide sequence that corresponds to an immediate-**early protein** gene or to a late protein gene operatively linked to an indicating means. The EcoRI J fragment of HCMV **DNA** was spliced into the EcoRI site of plasmid pUC18 and radiolabeled with 5'-(α-thio)-dATP-35S by nick translation. Strong hybridization with this probe was found in 2% of peripheral blood lymphocytes from 2 of 8 asymptomatic individuals who were seropos. for HCMV antibodies. A higher percentage of OKT4+ than OKT8+ lymphocytes showed hybridization with the probe.

L22 ANSWER 15 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 10 Aug 1985
ACCESSION NUMBER: 1985:432849 CAPLUS
DOCUMENT NUMBER: 103:32849
TITLE: **DNA** rearrangement in the control region for early transcription in a human polyomavirus JC host range mutant capable of growing in human embryonic **kidney** cells
AUTHOR(S): Miyamura, Tatsuo; Furuno, Akemi; Yoshike, Kunito
CORPORATE SOURCE: Dep. Enteroviruses, Natl. Inst. Health, Tokyo, 141, Japan
SOURCE: Journal of Virology (1985), 54(3), 750-6
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A human polyomavirus JC **virus** (JCV) host range mutant (JC-HEK)

can grow in human embryonic **kidney** cells, whereas the brain cell-tropic wild-type JCV strain (Mad-1) cannot; JC-HEK contains 2 complementing defective **DNAs**, JC-HEK-A and JC-HEK-B. The nucleotide sequence of the putative transcriptional control region of JC-HEK-A **DNA** that can induce T-antigen synthesis in human embryonic **kidney** cells was **determined** and compared with the sequence of JCV Mad-1 **DNA**. The JC-HEK-A control region had a complex **DNA** rearrangement, namely, a partial local duplication of a noncoding region generating the VP-1 gene (78 base pairs). In the rearranged segment, JC-HEK-A had 7 sets of the sequence 5'TGGA(T)A(T)A(T)3', which is found in the SV40 **virus** enhancer core, whereas JCV Mad-1 had only 1 set in its control region. JC-HEK-A also had a 5'TGGAAGTGTAA3' sequence resembling the **adenovirus early** region 1A enhancer core sequence 5'AGGAAGTGAA3'. Because the **viral** enhancer is host specific and because another human polyomavirus, BK **virus**, that grows well in human embryonic **kidney** cells has these signals in its control region, it is likely that some of the newly acquired signals in JC-HEK play an important role in the altered host range of JCV.

L22 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1982:539560 CAPLUS
DOCUMENT NUMBER: 97:139560
TITLE: The relationship between region E1a and E1b of human adenoviruses in cell transformation
AUTHOR(S): Van den Elsen, Peter; De Pater, Sylvia; Houweling, Ada; Van der Veer, Johan; Van der Eb, Alex
CORPORATE SOURCE: Dep. Med. Biochem., Sylvius Lab., Leiden, 2333 AL, Neth.
SOURCE: Gene (1982), 18(2), 175-85
CODEN: GENED6; ISSN: 0378-1119
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Baby rat **kidney** (BRK) cells were transfected either with intact region E1 **DNA** of adenovirus type 5 (Ad5) or with mixts. of **DNA** fragments containing the separated E1a and E1b regions. Mixts. of regions E1a and E1b transformed with a similar efficiency to that of intact region E1. **DNA** fragments containing region E1b alone had no **detectable** transforming activity in primary BRK cells or in established rat cell lines. When region E1a of Ad5 was combined with region E1b of Ad12, complete transformation was also obtained. Characterization of the cell lines transformed by separated E1a and E1b regions led to the following conclusions: (1) Expression of region E1b is not dependent on specific linkage to region E1a as it occurs in the intact E1 region. (2) Region E1b is normally expressed into the corresponding major adenovirus T antigens (65,000 and 19,000 mol. weight with region E1b of Ad5; 60,000 and 19,000 mol. weight with E1b of Ad12). (3) Region E1b of Ad12 can be activated by region E1a of Ad5, indicating that the E1a regions of both serotypes are functionally similar in transformation. (4) Cell lines containing region E1b of Ad5 are weakly oncogenic in nude mice, whereas cells containing E1b of Ad12 are highly oncogenic in nude mice, indicating that the

degree of oncogenicity is **determined** by region E1b.

L22 ANSWER 17 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1982:116770 CAPLUS
DOCUMENT NUMBER: 96:116770
TITLE: Effect of deletions in **adenovirus** **early** region 1 genes upon replication of adeno-associated **virus**
AUTHOR(S): Laughlin, Catherine A.; Jones, Nicholas; Carter, Barrie J.
CORPORATE SOURCE: Lab. Exp. Pathol., Natl. Inst. Arthritis, Diabetes Dig. Kidney Dis., Bethesda, MD, 20205, USA
SOURCE: Journal of Virology (1982), 41(3), 868-76
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The growth of adeno-associated **virus** (AAV) is dependent upon helper functions provided by adenovirus. The role of **adenovirus** **early** gene region 1 in the AAV helper function was investigated with 6 adenovirus type 5 (Ad5) host range mutants with deletions in early region 1. These mutants do not grow in human KB cells but are complemented by and grow in a line of adenovirus-transformed human embryonic **kidney** cells (293 cells); 293 cells contain and express the Ad5 early region 1 genes. Mutants with extensive deletions of **adenovirus early** region 1a (dl312) or regions 1a and 1b (dl313) helped AAV as efficiently as wild-type adenovirus in 293 cells, but neither mutant helped in KB cells. No AAV **DNA**, RNA, or protein synthesis was **detected** in KB cells in the presence of the mutant adenoviruses. Quant. blotting expts. showed that at 20 h after infection with AAV and either dl312 or dl313, there was <1 AAV genome/cell. In KB cells infected with AAV alone, the unreplicated AAV genomes were **detected** readily. Apparently, infection with adenovirus mutant dl312 or dl313 results in degradation of most of the infecting AAV genomes. At least an adenovirus region 1b product (and perhaps a region 1a product also) may be required for AAV **DNA** replication. This putative region 1b function appears to protect AAV **DNA** from degradation by an adenovirus-induced DNase. Addnl. Ad5 mutants (dl311, dl314, sub315, and sub316), were also tested. All of these mutants were inefficient helpers, and they showed varying degrees of multiplicity leakiness. The dl312 and dl313 complemented each other for the AAV helper function, and each was complemented by ad5ts125 at the nonpermissive temperature The defect in region 1 mutants for AAV helper function acts at a different stage of the AAV growth cycle than the defect in the region 2 mutant ts125.

L22 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1979:134947 CAPLUS
DOCUMENT NUMBER: 90:134947
TITLE: Nuclear accumulation of influenza **viral** RNA transcripts and the effects of cycloheximide, actinomycin D, and α-amanitin
AUTHOR(S): Mark, George E.; Taylor, J. M.; Broni, B.; Krug, R. M.
CORPORATE SOURCE: Fox Chase Cancer Cent., Inst. Cancer Res., Philadelphia, PA, USA

SOURCE: Journal of Virology (1979), 29(2), 744-52
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The use of **virus**-specific 32P-labeled complementary **DNA** and 125I-labeled virion RNA as hybridization probes has allowed quantitation of the number of mols. of complementary RNA (cRNA) and progeny virion RNA in MDCK (canine **kidney**) cells infected with influenza **virus**. The distribution of cRNA between the nucleus and the cytoplasm in cycloheximide-treated cells was compared to that found in untreated cells, beginning 1 h after infection. A greater percentage of the total cRNA was **detected** in the nucleus of the drug-treated cells at all times investigated. For the 1st 2 h after infection .apprx.50% of the cRNA synthesized in the cycloheximide-treated cells was in the nucleus. These nuclear cRNA mols. were characterized and shown to be polyadenylated transcripts of each of the genome virion RNA segments. **Viral** cRNA synthesis was not completely inhibited by the addition of actinomycin D at the beginning of infection, with or without the concomitant addition of cycloheximide. A large fraction (.apprx.90%) of these cRNA sequences was **detected** in the nucleus. These nuclear cRNA mols. contained polyadenylic acid and represented transcripts of both those segments coding for proteins synthesized predominantly early after infection (**early proteins**) and those virion RNA segments coding for late proteins. Also, in vitro translation of these cRNA mols. showed that they were functional **virus** mRNAs. In contrast to actinomycin D, α-amanitin completely inhibited cRNA synthesis when added at the beginning of infection, whereas addition of this drug after 1.5 h had no effect on further cRNA synthesis.

L22 ANSWER 19 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1978:148863 CAPLUS
DOCUMENT NUMBER: 88:148863
TITLE: The biological activity of different early simian **virus** 40 **DNA** fragments
AUTHOR(S): Graessmann, Monika; Graessmann, Adolf; Mueller, Christian
CORPORATE SOURCE: Inst. Molekularbiol. Biochem., Freie Univ. Berlin, Berlin, Fed. Rep. Ger.
SOURCE: Colloque INSERM (1977), 69(Early Proteins Oncogenic DNA Viruses), 233-9
CODEN: CINMDE; ISSN: 0768-3154
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Early functions of Simian **virus** 40 (SV40) were studied by mapping different early **viral DNA** fragments prepared by restriction endonuclease digestion and subsequent inoculation into primary mouse **kidney** cells and TC7 cells. The **determinant** group of the T antigen was located between map positions 0.375 and 0.655. Microinjection of the **viral DNA** fragment containing these positions induced a protein which reacted with T antigen sera. Cell **DNA** synthesis stimulation did not require the entire early SV40 genome. As the stimulation of **viral DNA** synthesis is a prerequisite for late **viral** gene expression, the function evidently requires expression of the total early **viral** genome. It is not known how cellular and **viral DNA** are

stimulated by SV40 **early protein**.

L22 ANSWER 20 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1969:35362 CAPLUS
DOCUMENT NUMBER: 70:35362
TITLE: Simian **virus** 40 **deoxyribonucleic** acid replication. I. Effect of cycloheximide on the replication of SV40 **deoxyribonucleic** acid in monkey **kidney** cells and in heterokaryons of SV40-transformed and susceptible cells
AUTHOR(S): Kit, Saul; Kurimura, Takashi; De Torres, Ramon A.; Dubbs, Del R.
CORPORATE SOURCE: Coll. of Med., Baylor Univ., Houston, TX, USA
SOURCE: Journal of Virology (1969), 3(1), 25-32
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Infectious **DNA** was extracted from green monkey **kidney** (CV-1) cultures at various times after the cultures were infected with simian **virus** 40 (SV40) at input multiplicities of 0.01 and 0.1 plaque-forming unit (PFU) per cell. A pronounced decrease in infectious **DNA** was observed 3-16 hrs. after **virus** infection, suggesting that structurally altered intracellular forms may have been generated early in infection. Evidence is also presented that SV40 **DNA** synthesis requires concurrent protein synthesis. **DNA** replication was studied in the presence and absence of cycloheximide in: SV40-infected and uninfected cultures of CV-1 cells; cultures synchronized with 1-β-D-arabinofuranosylcytosine (ara-C) 24-30 hrs. prior to the addition of cycloheximide; and in heterokaryons of SV40-transformed hamster and susceptible monkey **kidney** cells. **DNA** synthesis was **determined** by pulse-labeling the cultures with thymidine-3H at 24-46 hrs. after infection. In addition, the total infectious SV40 **DNA** was measured. Addition of cycloheximide, even after **early proteins** had been induced, grossly inhibited both SV40 and cellular **DNA** syntheses. The activities of thymidine kinase, **DNA** polymerase, deoxycytidylate deaminase, and thymidylate kinase were measured. These enzyme activities remained high for at least 9 hrs. in the presence of cycloheximide. SV40 **DNA** prelabeled with thymidine-3H before the addition of cycloheximide was also relatively stable during the time required for cycloheximide to inhibit further **DNA** replication.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 15:30:17 ON 11 FEB 2005)
L23 143 S L22
L24 129 S L23 AND CELL
L25 30 S L24 AND GENOM##
L26 49 S L23 AND HUMAN?(S)CELL
L27 70 S L25 OR L26
L28 46 DUP REM L27 (24 DUPLICATES REMOVED)

L28 ANSWER 1 OF 46 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 2005:63143 BIOSIS
DOCUMENT NUMBER: PREV200500061188

TITLE: Expression and localization of the Epstein-Barr **virus**-encoded protein kinase.
AUTHOR(S): Gershburg, E.; Marschall, M.; Hong, K.; Pagano, J. S. [Reprint Author]
CORPORATE SOURCE: Lineberger Comprehens Canc Ctr, Univ N Carolina, CB 7295, Chapel Hill, NC, 27599, USA
joseph_pagano@med.unc.edu
SOURCE: Journal of Virology, (November 2004) Vol. 78, No. 22, pp. 12140-12146. print.
ISSN: 0022-538X (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Feb 2005
Last Updated on STN: 9 Feb 2005

AB The protein kinase (PK) encoded by the Epstein-Barr **Virus** (EBV) BGLF4 gene is the only EBV protein kinase. The expression pattern of EBV PK during the reactivation of the **viral** lytic cycle and the subcellular localization of the protein were analyzed with a polyclonal antiserum raised against a peptide corresponding to the N terminus of EBV PK. Based on previously published data (E. Gershburg and J. S. Pagano, J. Virol. 76:998-1003, 2002) and the expression pattern described here, we conclude that EBV PK is an **early protein** that requires **viral-DNA** replication for maximum expression. By biochemical fractionation, the protein could be **detected** mainly in the nuclear fraction 4 h after **viral** reactivation in Akata cells. Nuclear localization could be visualized by indirect immunofluorescence in HeLa cells transiently expressing EBV BGLF4 in the absence of other **viral** products. Transient expression of 3'-terminal deletion mutants of EBV BGLF4 resulted in cytoplasmic localization, confirming the presence of a nuclear localization site in the C-terminal region of the protein. In contrast to the wild-type EBV PK, all of the mutants were unable to hyperphosphorylate EA-D during coexpression or to phosphorylate ganciclovir, as measured by an in-cell activity assay. Thus, the results demonstrate that the nuclear localization, as well as the kinase activity, of BGFL4 is dependent on an intact C-terminal region.

L28 ANSWER 2 OF 46 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2004308967 EMBASE
TITLE: Analysis of splice variants of the immediate-early 1 region of human cytomegalovirus.
AUTHOR: Awasthi S.; Isler J.A.; Alwine J.C.
CORPORATE SOURCE: J.C. Alwine, 314 Biomed. Research Building II/III, University of Pennsylvania, 421 Curie Blvd., Philadelphia, PA 19104, United States. alwine@mail.med.upenn.edu
SOURCE: Journal of Virology, (2004) 78/15 (8191-8200).
Refs: 30
ISSN: 0022-538X CODEN: JOVIAM
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
005 General Pathology and Pathological Anatomy
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The major immediate-early (MIE) gene of **human** cytomegalovirus

(HCMV) produces multiple mRNAs through differential splicing and polyadenylation. Reverse transcriptase PCR was used to characterize transcripts from exons 1, 2, 3, and 4 (immediate-early 1 [IE1]). The expected IE72 and IE19 mRNAs were **detected**, as well as two heretofore-uncharacterized transcripts designated IE17.5 and IE9. The IE72, IE19, and IE17.5 transcripts utilized the same 5'-splice site in exon 3. IE9 utilized a cryptic 5'-splice site within exon 3. The IE19, IE17.5, and IE9 transcripts all used different 3'-splice sites within exon 4. These spliced species occur in infected **human** foreskin fibroblast (HFF) **cells**, with accumulation kinetics similar to those of IE72 mRNA. IE19 and IE9 RNAs were much more abundant than IE17.5 RNA. Transfection of CV-1 **cells** with cDNAs resulted in IE19 and IE17.5 proteins **detectable** by antibodies to either N-terminal or C-terminal epitopes. No IE9 protein product has been **detected**. We have not been able to **detect** IE19, IE17.5, or IE9 proteins during infection of HFF, HEL, or U373MG **cells**. Failure to **detect** IE19 protein contrasts with a previous report (M. Shirakata, M. Terauchi, M. Ablikin, K. Imadome, K. Hirai, T. Aso, and Y. Yamanashi, J. Virol. 76:3158-3167, 2002) of IE19 protein expression in HCMV-infected HEL **cells**. Our analysis suggests that an N-terminal breakdown product of IE72 may be mistaken for IE19. Expression of IE19 or IE17.5 from its respective cDNA results in repression of **viral** gene expression in infected **cells**. We speculate that expression of these proteins during infection may be restricted to specific conditions or **cell** types.

L28 ANSWER 3 OF 46 MEDLINE on STN
ACCESSION NUMBER: 2003243751 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12766070
TITLE: Multiple **determinants** contribute to the virulence of HSV **ocular** and CNS infection and identification of serine 34 of the US1 gene as an **ocular** disease **determinant**.
AUTHOR: Brandt Curtis R; Kolb Aaron W; Shah Dipti D; Pumfery Anne M; Kintner Randall L; Jaehnig Eric; Van Gompel Jamie J
CORPORATE SOURCE: Departments of Ophthalmology and Visual Sciences, University of Wisconsin Medical School, Madison, Wisconsin 53706, USA.. crbrandt@facstaff.wisc.edu
CONTRACT NUMBER: EY07336 (NEI)
T3226M08349
SOURCE: Investigative ophthalmology & visual science, (2003 Jun) 44 (6) 2657-68.
Journal code: 7703701. ISSN: 0146-0404.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 20030528
Last Updated on STN: 20030613
Entered Medline: 20030612

AB PURPOSE: The virulence of any given strain of **herpes** simplex **virus** (**HSV**) is probably due to the effects of the constellation of genes in that strain and how they act in concert to promote disease. The goal of this work was to develop a system to identify and study the role of multiple genes in HSV disease. METHODS:

Mixed **ocular** infection with HSV-1 strains CJ394 and OD4 yield recombinants with increased **ocular** and central nervous system (CNS) virulence. Clones and subclones of the CJ394 **genome** were cotransfected with intact OD4 **DNA** into Vero **cells**, the transfection pools were inoculated into BALB/c mouse **eyes**, and disease severity was scored. Fragments transferring increased **ocular** or CNS disease were sequenced. Site-directed mutagenesis was used to revert one mutation to wild type. RESULTS: Five of the **determinants** (UL9, -33, -41, and -42 and US1) increased **ocular** disease when transferred singly. Transfer of the UL36/37 **determinant** increased both **ocular** and CNS disease. Transfer of the UL41 and -42 genes increased mortality and a combination of the UL36/37, -41, and -42 **determinants** increased virulence further. Reversion of the S34A change in the OD4 US1 gene to wild type restored **ocular** virulence. CONCLUSIONS: Multiple HSV genes can operate to increase virulence. The UL9, -33, -36/37, and -42 genes have not previously been identified as virulence **determinants**. The UL41 and US1 genes are known to affect disease, but the changes identified had not been described. Multiple novel mutations were found in the OD4, UL9, UL36, and US1 genes, and we showed that S34 in the US1 gene is essential in **ocular** disease.

L28 ANSWER 4 OF 46 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation. on STN

ACCESSION NUMBER: 2004:15429 SCISEARCH
THE GENUINE ARTICLE: 753XY
TITLE: Possible involvement of epidermodysplasia verruciformis human papillomaviruses in the immunopathogenesis of psoriasis: a proposed hypothesis
AUTHOR: Majewski S; Jablonska S (Reprint)
CORPORATE SOURCE: Warsaw Acad Med & Hosp, Dept Dermatol, Koszykowa 82A, PL-02008 Warsaw, Poland (Reprint); Warsaw Acad Med & Hosp, Dept Dermatol & Venereol, Warsaw, Poland
COUNTRY OF AUTHOR: Poland
SOURCE: EXPERIMENTAL DERMATOLOGY, (DEC 2003) Vol. 12, No. 6, pp. 721-728.
Publisher: BLACKWELL MUNKSGAARD, 35 NORRE SOGADE, PO BOX 2148, DK-1016 COPENHAGEN, DENMARK.
ISSN: 0906-6705.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 56

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We have shown previously in psoriasis a very high prevalence of epidermodysplasia verruciformis-associated **human** papillomavirus 5 (EVHPV5) **DNA** and antibodies to **human** papillomavirus 5 (HPV5) **virus**-like particle (VLP)L1, and we suggested that this benign hyperproliferative disorder could be a reservoir for EVHPVs. Here we provide new data confirming the expression of EVHPVs in psoriasis and present our hypothesis on their possible involvement in the immunopathogenesis of the disorder. The new important finding was **detection** by a radioimmunoprecipitation assay of a very high prevalence of antibodies to E6/E7 HPV5 oncoproteins, known to enhance keratinocyte proliferation. More recently, EV genes were identified, EVER1 and EVER2, whose mutations are responsible for epidermodysplasia verruciformis. Epidermodysplasia verruciformis-associated **human**

papillomaviruses are harmless to the general population as a result of genetic restriction, which in psoriasis appears to be partly alleviated, and this may allow the **viral** gene expression. We hypothesize that induction of keratinocyte proliferation in psoriasis by various stimuli initiates the EVHPV life cycle with expression of early (E6/E7) and late (L1) **viral** proteins. The **early proteins** may, in turn, enhance the keratinocyte proliferation, and the late proteins could serve as a target for specific B- and T-**cell**-mediated responses. Immune responses against the **viral** antigens in the epidermis may result in chemoattraction of leukocytes and Munro abscess formation, as well as in production of proinflammatory cytokines, leading to self perpetuation of the psoriatic process. The novel immunomodulatory therapies could also inhibit immune responses against EVHPV proteins, leading to decreased cytokine production, keratinocyte proliferation and EVHPV expression. Thus the beneficial effect of these therapies is not discordant with the proposed hypothesis of possible involvement of EVHPVs in the immunopathogenesis of psoriasis.

L28 ANSWER 5 OF 46 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2003092822 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12604816
TITLE: **Detection** of **human** cytomegalovirus **DNA** replication in non-permissive Vero and 293 **cells**.
AUTHOR: Ellsmore Victoria; Reid G Gordon; Stow Nigel D
CORPORATE SOURCE: MRC Virology Unit, Institute of Virology, Church Street, Glasgow G11 5JR, Scotland, UK.
SOURCE: Journal of general virology, (2003 Mar) 84 (Pt 3) 639-45. Journal code: 0077340. ISSN: 0022-1317.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 20030227
Last Updated on STN: 20030328
Entered Medline: 20030327

AB Human cytomegalovirus (HCMV) displays an exceptionally restricted host range in tissue culture with human fibroblasts being the principal fully permissive system. Nevertheless, immediate early (IE) proteins are expressed following infection of many non-permissive **cell** types of **human**, simian and murine origin, and **viral** origin-dependent **DNA** synthesis has been reconstituted by transfection of plasmids into Vero **cells**, a non-permissive line from African green monkey. We have examined the accumulation of HCMV strain AD169 **DNA**, and the replication of transfected HCMV origin-containing plasmids, in infected Vero and **human** embryonic **kidney** 293 **cells**, which were previously reported to express the major IE protein in a small proportion of infected **cells** but to be non-permissive for **viral DNA** synthesis. In Vero cells accumulation of origin-containing plasmid but not **viral DNA** occurred, whilst in 293 cells both **DNAs** accumulated. Immunofluorescence experiments indicated that following infection with 3 p.f.u. per cell, a small fraction of both cell types expressed the UL44 **DNA** replication protein. Neither cell

line, however, supported the generation of infectious progeny **virus**. These results suggest that IE proteins expressed in Vero and 293 cells can induce the synthesis of **early proteins** capable of functioning in **viral DNA** replication, but there is a failure in later events on the pathway to infectious **virus** production. This provides further support for transfected Vero cells being a valid system in which to study HCMV **DNA** synthesis, and suggests that 293 cells may also prove useful in similar experiments.

L28 ANSWER 6 OF 46 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-112002 [10] WPIDS
DOC. NO. NON-CPI: N2003-089142
DOC. NO. CPI: C2003-028693
TITLE: **Determining** whether a compound influences a phase in the life cycle of a **virus**, useful for identifying antiviral compounds, by providing a **cell** with elements of the **virus** to perform the phase, and providing the **cell** with the compound.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): BRUS, R H P; SCHOUTEN, G J; UYTDEHAAG, A G C M
PATENT ASSIGNEE(S): (CRUC-N) CRUCELL HOLLAND BV
COUNTRY COUNT: 101
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002090982	A1	20021114	(200310)*	EN	70
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW					
EP 1256803	A1	20021113	(200310)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
EP 1388008	A1	20040211	(200411)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
US 2004086850	A1	20040506	(200430)		
AU 2002306089	A1	20021118	(200452)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2002090982	A1		WO 2002-NL296	20020506
EP 1256803	A1		EP 2001-201657	20010507
EP 1388008	A1		EP 2002-733606	20020506
			WO 2002-NL296	20020506
US 2004086850	A1	Cont of	WO 2002-NL296	20020506
			US 2003-698086	20031030
AU 2002306089	A1		AU 2002-306089	20020506

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1388008	A1 Based on	WO 2002090982
AU 2002306089	A1 Based on	WO 2002090982

PRIORITY APPLN. INFO: US 2001-289541P 20010507; EP 2001-201657 20010507

AN 2003-112002 [10] WPIDS

AB WO 200290982 A UPAB: 20030211

NOVELTY - **Determining** (M1) whether a compound influences a phase in the life cycle of a **virus** comprising providing a **cell** with at least the elements of the **virus** sufficient to perform the phase and the compound, and **determining** whether the phase is influenced by the compound, where the **cell** comprises a **nucleic** acid encoding an **adenovirus early protein** or its functional part, derivative and/or analog, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) identifying (M2) a compound with antiviral activity; and

(2) **determining** (M3) the effect of the absence of the compound on a phase in the life cycle of a **virus** by:

(a) culturing a **cell** otherwise capable of supporting the phase in the life cycle of a **virus** in the presence of the **virus** under conditions conducive to the phase in the life cycle in the absence of the compound; and

(b) examining the effect of the absence of the compound on the phase in the life cycle of the **virus**.

ACTIVITY - Virucide.

No biological data given.

MECHANISM OF ACTION - None given.

USE - The methods are useful for identifying antiviral compounds. The **cell** is useful for **screening** of a compound or library of compounds for their ability of influencing a phase in the life cycle of a **virus** capable of performing the phase in the **cell** (claimed).

Dwg.0/17

L28 ANSWER 7 OF 46 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2002-329795 [36] WPIDS

DOC. NO. NON-CPI: N2002-258824

DOC. NO. CPI: C2002-095357

TITLE: Identifying novel epitopes and binding molecules which bind the epitopes, used in treating e.g. cancer, by selecting a molecule from a library which binds diseased cells and identifying an epitope which binds the molecule.

DERWENT CLASS: B04 D16 P13 P14 S03

INVENTOR(S): BLOEM, A C; CILENTI, L; LOGTENBERG, T; ZWIJSEN, R M L; ZWIJSSEN, R M L

PATENT ASSIGNEE(S): (CRUC-N) CRUCELL HOLLAND BV; (UBIS-N) U-BISYS BV; (BLOE-I) BLOEM A C; (CILE-I) CILENTI L; (LOGT-I) LOGTENBERG T; (ZWIJ-I) ZWIJSEN R M L

COUNTRY COUNT: 98

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002018948	A2	20020307	(200236)*	EN	130
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
EP 1184458	A1	20020306	(200236)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
AU 2001094373	A	20020313	(200249)		
US 2002115065	A1	20020822	(200258)		
EP 1356285	A2	20031029	(200379)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002018948	A2	WO 2001-NL636	20010827
EP 1184458	A1	EP 2000-202991	20000828
AU 2001094373	A	AU 2001-94373	20010827
US 2002115065	A1 Provisional	US 2000-228429P	20000828
		US 2001-940386	20010827
EP 1356285	A2	EP 2001-975003	20010827
		WO 2001-NL636	20010827

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001094373	A	Based on	WO 2002018948
EP 1356285	A2	Based on	WO 2002018948

PRIORITY APPLN. INFO: US 2000-228429P 20000828; EP 2000-202991 20000828; US 2001-940386 20010827

AN 2002-329795 [36] WPIDS

AB WO 200218948 A UPAB: 20020610

NOVELTY - Identifying (I) a disease associated molecular marker or novel epitope associated with a subset of cells, is new.

DETAILED DESCRIPTION - Identifying a disease associated molecular marker or novel epitope associated with a subset of cells comprises:

(a) incubating the cells of a species with a library of binding molecules (BM), combined with an incubation with diseased cells (DC) of the species;

(b) obtaining from the incubation, a collection of DC essentially free from non-DC, by sorting the collection of DC from non-DC according to parameters which distinguish between the collection of DC and the non-DC;

(c) obtaining BMs from the collection of DC;

(d) selecting from the obtained BMs, an individual BM capable of preferential binding to the DC as compared to binding to the non-DC;

(e) identifying a molecular marker which, in its disease associated form, binds to individual BM, the molecular marker being associated with the collection of DC obtainable in (b); and

(f) establishing that the disease associated form has a counterpart associated with non-DC, where the counterpart is less capable of binding the individual BM.

INDEPENDENT CLAIMS are also included for the following:

(1) identifying (II) a BM capable of binding a subset of DC, by performing (a)-(d) as above, recovering the individual BM and establishing that the individual BM preferentially binds to a molecular marker in its disease associated form associated with the DC, the molecular marker further has a counterpart associated with non-DC;

(2) a disease associated molecular marker or novel epitope obtained by (I) or (II);

(3) a BM (III) obtained by (I) or (II);

(4) a BM (IV) capable of specifically binding to an epitope present in a subset of CD46 proteins;

(5) use of an epitope expressed on a subset of CD46 expressing cells as a marker for neoplastic cells;

(6) a **nucleic** acid (V) encoding (III) or (IV), or its part;

(7) a cell (VI) comprising (V);

(8) a plant or a non-human animal (VII) comprising (VI);

(9) a gene delivery vehicle (VIII) comprising (V); and

(10) a kit comprising (III) or (IV).

ACTIVITY - Cytostatic.

The anti-tumor effect of K53/IgG1 was evaluated. Seven week-old Balb/c (nu/nu) mice were injected subcutaneously into both flanks with 1 multiply 106 LS174T cells. On day 1, 6 and 9, three groups of 5 animals were treated with 300 micro g antibody. One group with K53/IgG1, one with GBSIII (negative control) and one with UBS-54 (positive control). On day 3 and 6 (group A), 9 and 12 (group B) and 12 and 15 (group C), the treatment was repeated with 150 micro g antibody. K53/IgG1 produced in BHK-21 cells was used for the antibody treatment on day 1. A mixture of K53/IgG1 produced in HEK 293 cells and K53/IgG1 produced in BHK-21 cells were used for the antibody treatment on day 9. Treatment effects were evaluated by measuring the mean tumor size on day 9, 13, 15, 17 (group A and B) or day 18 (group C). When the K53/IgG1 antibody treatment started on day 1 (group A), the tumor growth was significantly retarded when compared to the tumor growth in mice treated with the control antibody GBS III. After 17 days, only 3 mice developed a tumor. Also when the antibody treatment was started at day 6 or 9 (group B and C respectively) there was a clear tendency of tumor growth retardation when the animals were treated with K53/IgG1 or UBS-54, compared to the mice treated with the negative control antibody GBS III. Although, there was no difference in the number of mice that developed a tumor, the size of the tumors in the K53/IgG1 and UBS-54 treated mice was smaller than the tumors of the GBS III treated mice. These results showed that when the K53/IgG1 antibody treatment was started immediately, the number of animals developing a tumor was reduced by 70%. Only 3 mice developed a tumor, whereas in the GBS III control group all animals developed a tumor.

MECHANISM OF ACTION - Antibody-based therapy; CD46 binding.

USE - (I) is useful for identifying a novel epitope or disease-associated molecular marker associated with a subset of **cells**. (II) is useful for identifying a BM capable of binding a subset of DC. (III) and (IV) are useful for treating an individual suffering from or at risk of suffering from a disease, especially a

neoplastic disease and for preparing a medicament for treating neoplastic disease. (III) and (IV) are also useful for typing a **cell**, by **determining** whether the **cell** is capable of specifically binding to the BM. (IV) is capable of distinguishing a subset of CD46 comprising **cells** such as hemopoietic **cell** derived from B-**cells**, cervix, colon, **kidney** or liver **cells** (claimed). Purified BMs are also useful for preparation of diagnostic tools, and are useful to diagnose, prevent and/or treat different kinds of **human** malignancies, in particular multiple myeloma. (VIII) is useful to target delivery of **nucleic** acids to DC expressing a post-translationally modified protein belonging to a subset of proteins, such as the CD46 protein.

ADVANTAGE - The method provides a new way of searching for disease associated molecular markers which would not be identified using conventional means.

Dwg.0/28

L28 ANSWER 8 OF 46 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN

ACCESSION NUMBER: 2002:220744 BIOSIS
DOCUMENT NUMBER: PREV200200220744
TITLE: The immediate-**early protein**, ICPO, is essential for the resistance of **herpes** simplex **virus** to interferon-alpha/beta.
AUTHOR(S): Harle, Peter; Sainz, Bruno, Jr.; Carr, Daniel J. J.; Halford, William P. [Reprint author]
CORPORATE SOURCE: Department of Microbiology and Immunology, Tulane University Medical School, 1430 Tulane Avenue, SL-38, New Orleans, LA, 70112, USA
halford@tulane.edu
SOURCE: Virology, (February 15, 2002) Vol. 293, No. 2, pp. 295-304. print.
CODEN: VIRLAX. ISSN: 0042-6822.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Apr 2002
Last Updated on STN: 3 Apr 2002

AB **Herpes** simplex **virus** type 1 (**HSV**-1) is resistant to the antiviral effects of interferon (IFN)-alpha, -beta, or -gamma. The fact that ICPO- mutants replicate like wild-type **virus** in IFN-alpha/beta receptor knockout mice (Leib et al., 1999, J. Exp. Med. 189, 663) suggested that ICPO may serve a direct role in the resistance of HSV-1 to IFN. To test this hypothesis, the effects of IFN-alpha, -beta, and -gamma were compared against wild-type HSV-1 and an ICPO- mutant **virus**, 7134. In Vero **cells**, 7134 was more sensitive to inhibition by low doses of type I IFN (-alpha/beta) or type II IFN (-gamma) than vesicular stomatitis **virus**, a well-studied IFN-sensitive **virus**. At a concentration of 100 U/ml, IFN-alpha, -beta, or -gamma reduced the efficiency of 7134 plaque formation by 120-, 560-, and 45-fold, respectively. In contrast, none of the IFNs reduced wild-type HSV-1 plaque formation by more than 3-fold. Even when Vero **cells** were infected with 10 pfu per **cell**, IFN-alpha and -beta inhibited 7134 replication by over 100-fold, but inhibition by IFN-gamma decreased to less than 10-fold. While IFN-beta efficiently inhibited 7134 replication in primary mouse **kidney** and SK-N-SH **cells**, IFN-gamma did not inhibit 7134 to a

comparable extent in these **cells**. ICPO provided in trans from an adenovirus vector allowed 7134 to replicate efficiently in Vero **cells** in the presence of IFN-alpha, -beta, or -gamma. While IFN-beta or -gamma efficiently repressed the ICPO promoter-lacZ reporter gene in 7134 (i.e., apprx60-fold reduction in beta-galactosidase activity), ICPO provided in trans almost completely reversed IFN-mediated repression of the lacZ gene in 7134. The results suggest that the rate of ICPO expression in infected **cells** in vivo may be critical in **determining** whether host IFNs repress the HSV-1 **genome**. This concept is discussed in light of its potential relevance to the establishment of latent HSV-1 infections.

L28 ANSWER 9 OF 46 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN

ACCESSION NUMBER: 2001:452597 BIOSIS
DOCUMENT NUMBER: PREV200100452597
TITLE: The cellular protein PRA1 modulates the anti-apoptotic activity of Epstein-Barr **virus** BHRF1, a homologue of Bcl-2, through direct interaction.
AUTHOR(S): Li, Long-Yuan; Shih, Hsiu-Ming; Liu, Mei-Ying; Chen, Jen-Yang [Reprint author]
CORPORATE SOURCE: College of Medicine, Graduate Institute of Microbiology, National Taiwan University, Jen-Ai Road, Rm. 743, Number 1, Section 1, Taipei, Taiwan
cjy@nhri.org.tw
SOURCE: Journal of Biological Chemistry, (July 20, 2001) Vol. 276, No. 29, pp. 27354-27362. print.
CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Sep 2001
Last Updated on STN: 22 Feb 2002

AB The Epstein-Barr **virus**-encoded **early protein**, BHRF1, is a structural and functional homologue of the anti-apoptotic protein, Bcl-2. There is accumulating evidence that BHRF1 protects a variety of cell types from apoptosis induced by various external stimuli. To identify specific proteins from normal epithelial **cells** that interact with BHRF1 and that might promote or inhibit its anti-apoptotic activity, we **screened** a yeast two-hybrid cDNA library derived from **human** normal foreskin keratinocytes and identified a cellular gene encoding **human** prenylated rab acceptor 1 (hPRA1). The interaction of hPRA1 with BHRF1 was confirmed using glutathione S-transferase pull-down assays, confocal laser scanning microscopy, and co-immunoprecipitation. Two regions of PRA1, amino acids 30-53 and the carboxyl-terminal 21 residues, are important for BHRF1 interactions and two regions of BHRF1, amino acids 1-18 and 89-142, including the Bcl-2 homology domains BH4 and BH1, respectively, are crucial for PRA1 interactions. PRA1 expression interferes with the anti-apoptotic activity of BHRF1, although not of Bcl-2. These results indicate that the PRA1 interacts selectively with BHRF1 to reduce its anti-apoptotic activity and might play a role in the impeding completion of **virus** maturation.

L28 ANSWER 10 OF 46 JICST-EPlus COPYRIGHT 2005 JST on STN
ACCESSION NUMBER: 1010922217 JICST-EPlus
TITLE: A Rabbit Model for Human Cytomegalovirus Retinitis.

AUTHOR: MATSUDA YOSHITO; SAKURAI EIJI; OZEKI HIRONORI; KUNO NORIYUKI; OGURA YUICHIRO
NAKAJIMA KATSUHISA
CORPORATE SOURCE: Nagoyashidai I Ganka
Nagoyashidai I Uirusugaku
SOURCE: Nippon Ganka Gakkai Zasshi (Journal of Japanese Ophthalmological Society), (2001) vol. 105, no. 9, pp. 597-602. Journal Code: Z0666A (Fig. 5, Ref. 22)
ISSN: 0029-0203
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New

AB Purpose: To develop a rabbit model for **human** cytomegalovirus (HCMV) retinitis. Methods: 0.1 ml of 1*106 plaque forming units/ml HCMV was injected into the vitreous cavity of 10 pigmented rabbit **eyes**. The **eyes** were examined ophthalmoscopically on days 1, 2, 3, 4 and 7 and once a week thereafter until 4 weeks after inoculation. Vitreal and **retinal** findings were graded from 0+ to 4+ on a scale of increasing severity. In addition, we examined the enucleated **eyes** 3 weeks after HCMV inoculation by histological and immunohistochemical techniques. Results: All injected **eyes** developed vitreoretinal lesions. Vitreous opacities appeared the next day and increased until 4 days after HCMV inoculation. Whitish **retinal** exudates occurred on day 3 and increased until 3 weeks after HCMV inoculation. Vitreoretinal lesions then disappeared by 4 weeks after inoculaion. Histological examination revealed intraretinal infiltration of inflammatory **cells** and disorganization of the inner **retinal** architecture. HCMV antigens were **detected** inside the **retina** by immunofluorescence using anti **early protein** antibody against HCMV. Conclusions: The results indicate that this rabbit model can be useful to develop and evaluate a new treatment modality for cytomegalovirus retinitis. (author abst.)

L28 ANSWER 11 OF 46 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2000387834 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10846077
TITLE: Optimized **viral** dose and transient immunosuppression enable **herpes** simplex **virus** ICP0-null mutants To establish wild-type levels of latency in vivo.
AUTHOR: Halford W P; Schaffer P A
CORPORATE SOURCE: Department of Microbiology, University of Pennsylvania School of Medicine, Philadelphia 19104-6076, USA.
CONTRACT NUMBER: AI 10147 (NIAID)
P01 NS 35138 (NINDS)
SOURCE: Journal of virology, (2000 Jul) 74 (13) 5957-67.
Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000818
Last Updated on STN: 20000818
Entered Medline: 20000810

Searcher : Shears 571-272-2528

AB The reduced efficiency with which **herpes** simplex **virus** type 1 (**HSV**-1) mutants establish latent infections in vivo has been a fundamental obstacle in efforts to **determine** the roles of individual **viral** genes in **HSV**-1 reactivation. For example, in the absence of the "nonessential" **viral** immediate-**early protein**, ICP0, HSV-1 is severely impaired in its ability to (i) replicate at the site of inoculation and (ii) establish latency in neurons of the peripheral nervous system. The mouse **ocular** model of HSV latency was used in the present study to **determine** if the conditions of infection can be manipulated such that replication-impaired, ICP0-null mutants establish wild-type levels of latency, as measured by **viral genome** loads in latently infected trigeminal ganglia (TG). To this end, the effects of inoculum size and transient immunosuppression on the levels of acute replication in mouse **eyes** and of **viral DNA** in latently infected TG were examined. Following inoculation of mice with 2 x 10(3), 2 x 10(4), 2 x 10(5), or 2 x 10(6) PFU/**eye**, wild-type **virus** replicated in mouse **eyes** and established latency in TG with similar efficiencies at all four doses. In contrast, increasing the inoculum size of the ICP0-null mutants n212 and 7134 from 2 x 10(5) to 2 x 10(6) PFU/**eye** significantly decreased the levels of infectious **virus detected** in the tear films of mice from days 4 to 9 postinfection. In an attempt to establish the biological basis for this finding, the effect of **viral** dose on the induction of the host proinflammatory response was examined. Quantitative reverse transcription-PCR demonstrated that increasing the inoculum of 7134 from 2 x 10(4) to 2 x 10(6) PFU/**eye** significantly increased the expression of proinflammatory (interleukin 6), **cell** adhesion (intercellular adhesion molecule 1), and phagocyte-associated (CD11b) genes in mouse **eyes** 24 h postinfection. Furthermore, transient immunosuppression of mice with cyclophosphamide, but not cyclosporin A, significantly enhanced both the levels of acute n212 and 7134 replication in the **eye** and the levels of mutant **viral genomes** present in latently infected TG in a dose-dependent manner. Thus, the results of this study demonstrate that acute replication in the **eye** and the number of ICP0-null mutant **genomes** in latently infected TG can be increased to wild-type levels for both n212 and 7134 by (i) optimization of inoculum size and (ii) transient immunosuppression with cyclophosphamide.

L28 ANSWER 12 OF 46 MEDLINE on STN
ACCESSION NUMBER: 1998216793 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9557715
TITLE: A **virus** with a mutation in the ICP4-binding site in the L/ST promoter of **herpes** simplex **virus** type 1, but not a **virus** with a mutation in open reading frame P, exhibits cell-type-specific expression of gamma(1)34.5 transcripts and latency-associated transcripts.
AUTHOR: Lee L Y; Schaffer P A
CORPORATE SOURCE: Dana-Farber Cancer Institute and Department of Microbiology and Molecular Genetics, Harvard Medical School, Boston, Massachusetts 02115, USA.
CONTRACT NUMBER: P01 NS35138 (NINDS)
R37 CA20260 (NCI)
SOURCE: Journal of virology, (1998 May) 72 (5) 4250-64.

Searcher : Shears 571-272-2528

Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980529
Last Updated on STN: 19980529
Entered Medline: 19980520

AB The **herpes** simplex **virus** type 1 L/S junction-spanning transcripts (L/STs) are a family of multisized transcripts expressed at high levels in cells infected with mutant **viruses** that (i) do not express ICP4, (ii) specify forms of ICP4 unable to bind to the consensus ICP4 binding site, or (iii) contain mutations in the ICP4 binding site located at the transcriptional start site of the L/STs. By extension, the failure to **detect** the L/STs in wild-type **virus**-infected cells is due to the repressive effect of ICP4 bound to its cognate binding site upstream of the L/ST transcription initiation site. ORF-P, the first and largest open reading frame (ORF) encoded by the L/STs, overlaps >90% of the ORF encoding ORF-34.5, a putative neurovirulence factor, which is transcribed from the opposite **DNA** strand. **Viruses** with mutations in the overlapping region of ORF-P and ICP34.5 exhibit premature shutoff of infected-cell protein synthesis and are highly attenuated following intracranial inoculation of juvenile mice. To **determine** whether the premature protein shutoff and neuroattenuated phenotypes of ORF-P ORF-34.5 double mutants are a consequence of alterations in ORF-P, ORF-34.5, or both, **viruses** containing mutations only in ORF-P or only in the ICP4 binding site in the L/ST promoter were isolated and characterized. Mutant **virus** L/ST-n38 contains a single-base-pair transition mutation in ORF-P codon 38, resulting in translational termination of the ORF-P protein (OPP). This mutation does not alter the amino acid sequence of ICP34.5. Expression of a truncated form of OPP by mutant **virus** L/ST-n38 did not result in premature shutoff of infected-cell protein synthesis and produced no other observable phenotype relative to wild-type **virus** in in vitro tests. Moreover, the 50% lethal dose (LD50) of L/ST-n38 was comparable to that of wild-type **virus** following intracranial inoculation of 3-week-old mice, as were the latency and reactivation phenotypes of the **virus**. These properties of L/ST-n38 indicate that the attenuated phenotype of ORF-P ORF-34.5 double mutants is a consequence of mutations that affect the function of ICP34.5 and not the function of OPP. Mutant **virus** LST-4BS contains four single-base-pair substitutions in the ICP4 binding site in the L/ST promoter that abrogate the binding of ICP4 to this site, leading to high-level expression of the L/STs and OPP. LST-4BS induced premature shutoff of **viral** and cellular protein synthesis and was slightly growth restricted in **cells** of neural lineage (SK-N-SH **human** neuroblastoma **cells**) but was wild type for these two parameters in **cells** of nonneural lineage (immortalized primate Vero **cells**). Of particular interest was the observation that L/ST-4BS exhibited cell-type-specific expression of both the gamma(1)34.5 transcripts and the latency-associated transcripts (LATs). Thus, expression of these transcripts was barely **detectable** in cells of neural lineage (NB41A3 mouse neuroblastoma cells) but was wild type in Vero cells. In vivo, L/ST-4BS was reactivated from mouse trigeminal ganglia with reduced efficiency and delayed kinetics relative

to wild-type **virus**. L/ST-4BS was completely attenuated for neurovirulence (LD50 > 10(6) PFU) relative to wild-type **virus** (LD50 < 900 PFU), although the four single-base-pair substitutions lie outside the coding region for the neurovirulence factor, ICP34.5. Collectively, the complex in vitro and in vivo phenotypes of L/ST-4BS can be attributed to (i) disruptions of the ICP4 binding site in the L/ST promoter and subsequent overexpression of the L/STs and OPP; (ii) alterations in ORF-O, which is also mutated in L/ST-4BS; or (iii) alterations in other cryptic genes or cis-acting elements.

L28 ANSWER 13 OF 46 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 1999067976 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9850990
TITLE: Pseudorabies **virus** (PRV) **early protein** 0 activates PRV gene transcription in combination with the immediate-**early protein** IE180 and enhances the infectivity of PRV **genomic DNA**.
AUTHOR: Ono E; Watanabe S; Nikami H; Tasaki T; Kida H
CORPORATE SOURCE: Laboratory of Animal Experiments, Hokkaido University, Sapporo, Japan.. etsuro@imm.hokudai.ac.jp
SOURCE: Veterinary microbiology, (1998 Oct) 63 (2-4) 99-107. Journal code: 7705469. ISSN: 0378-1135.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990216
Last Updated on STN: 19990216
Entered Medline: 19990204

AB Pseudorabies **virus** (PRV) **early protein** 0 (EP0) functions as a transactivator of the **viral** gene promoters. In transient expression assays employing chloramphenicol acetyl transferase (CAT) reporter constructs, EP0 and the immediate-**early protein** IE180 act in an additive manner to activate transcription from the thymidine kinase (TK) and glycoprotein G (gG) gene promoters. EP0 enhanced the synthesis of infectious **virus** in cotransfection experiments with the EP0-expression plasmid and PRV **genomic DNA**. EP0 was **detected** by Western blot analysis in the purified virions. These results may indicate that EP0 in the virions acts as an important transactivator to express the immediate-early gene efficiently in the first stage of infection, and IE180 and EP0 expressed after the infection cooperatively activate the early and late gene expression in the later stage of infection.

L28 ANSWER 14 OF 46 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 97250539 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9096395
TITLE: Human cytomagalovirus IE1 and IE2 proteins are mutagenic and mediate "hit-and-run" oncogenic transformation in cooperation with the adenovirus E1A proteins.
AUTHOR: Shen Y; Zhu H; Shenk T
CORPORATE SOURCE: Department of Molecular Biology, Princeton University, NJ 08544-1014, USA.
CONTRACT NUMBER: CA41086 (NCI)

SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1997 Apr 1) 94 (7) 3341-5. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970514
Last Updated on STN: 19970514
Entered Medline: 19970508

AB Some epidemiological studies have suggested a possible link between **human** cytomegalovirus (HCMV) infection and various malignancies, and HCMV has been shown to transform cultured **cells**. However, **viral DNA** is not **detected** in most transformants, and the mechanism by which HCMV might contribute to oncogenesis has remained obscure. Here we show that the HCMV immediate early 1 and 2 genes can cooperate with the adenovirus E1A gene to generate transformed foci of primary baby rat **kidney** cells. HCMV gene expression is transient and **viral DNA** is not present in clonal cell lines derived from the transformed foci. We find that the HCMV immediate **early proteins** are mutagenic, and we propose that HCMV has the potential to contribute to oncogenesis through a "hit-and-run" mechanism, by inducing mutations in cellular genes.

L28 ANSWER 15 OF 46 MEDLINE on STN
ACCESSION NUMBER: 1998336496 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9672625
TITLE: Enhanced cytopathic effect of **human** cytomegalovirus on a **retinal** pigment epithelium **cell** line, K-1034, by serum-free medium.
AUTHOR: Ando Y; Iwasaki T; Sata T; Soushi S; Kurata T; Arao Y
CORPORATE SOURCE: Department of Pathology, National Institute of Infectious Diseases, Tokyo, Japan.
SOURCE: Archives of virology, (1997) 142 (8) 1645-58. Journal code: 7506870. ISSN: 0304-8608.
PUB. COUNTRY: Austria
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 19980817
Last Updated on STN: 19980817
Entered Medline: 19980806

AB Although **human** cytomegalovirus (HCMV) predominantly infects epithelial **cells** in vivo, the majority of studies of HCMV gene expression and replication have been conducted using non-epithelial **cell** lines in part because of the absence of a good experimental system using epithelial **cells**. To address the nature of epithelial **cell** infection, we investigated the susceptibility of an epithelial **cell** line (K-1034) established from the **retinal** pigment epithelium to HCMV infection. This **cell** line exhibited high susceptibility to HCMV, as evidenced by **detection** of one of the immediate early antigens, IE2, in the nuclei of more than 80% of K-1034 **cells** at 24 h following inoculation at a multiplicity of infection of 3 plaque forming units per

cell. However, the yield after one-step growth of HCMV in K-1034 **cells** was about twenty-fold less than that in **human** embryonic lung fibroblast **cells**. Cytopathic effect (CPE) on K-1034 **cells** was not prominent in medium supplemented with 10% fetal bovine serum and **viral** late antigens were **detected** in less than 5% of K-1034 **cells**. Interestingly, infected **cells** expressing late antigens and exhibiting CPE were markedly increased in serum-free medium, even though the yield of infectious HCMV and **viral genome** copy numbers were almost the same in the different serum concentrations, due to **viral** instability in the absence of serum. Thus, the progression of late antigens expression and the induction of CPE in infected epithelial **cells** is influenced by physiological conditions, and are negatively regulated by some serum factor.

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ACCESSION NUMBER: 1996:456939 BIOSIS
DOCUMENT NUMBER: PREV199699179295
TITLE: **Adenovirus early** region 4 34-kilodalton protein directs the nuclear localization of the early region 1B 55-kilodalton protein in primate cells.
AUTHOR(S): Goodrum, Felicia D.; Shenk, Thomas; Ornelles, David A. [Reprint author]
CORPORATE SOURCE: Dep. Microbiol. Immunol., Bowman Gray Sch. Med. Wake Forest Univ., Winston-Salem, NC 27157-1064, USA
SOURCE: Journal of Virology, (1996) Vol. 70, No. 9, pp. 6323-6335. CODEN: JOVIAM. ISSN: 0022-538X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Oct 1996
Last Updated on STN: 11 Oct 1996

AB The localization of the adenovirus type 5 34-kDa E4 and 55-kDa E1B proteins was **determined** in the absence of other adenovirus proteins. When expressed by transfection in **human**, monkey, hamster, rat, and mouse **cell** lines, the E1B protein was predominantly cytoplasmic and typically was excluded from the nucleus. When expressed by transfection, the E4 protein accumulated in the nucleus. Strikingly, when coexpressed by transfection in **human**, monkey, or baby hamster **kidney cells**, the E1B protein colocalized in the nucleus with the E4 protein. A complex of the E4 and E1B proteins was identified by coimmunoprecipitation in transfected HeLa cells. By contrast to the interaction observed in primate and baby hamster **kidney** cells, the E4 protein failed to direct the E1B protein to the nucleus in rat and mouse cell lines as well as CHO and V79 hamster cell lines. This failure of the E4 protein to direct the nuclear localization of the E1B protein in REF-52 rat cells was overcome by fusion with HeLa cells. Within 4 h of heterokaryon formation and with protein synthesis inhibited, a portion of the E4 protein present in the REF-52 nuclei migrated to the HeLa nuclei. Simultaneously, the previously cytoplasmic E1B protein colocalized with the E4 protein in both **human** and rat **cell** nuclei. These results suggest that a primate cell-specific factor mediates the functional interaction of the E1B and E4 proteins of adenovirus.

L28 ANSWER 17 OF 46 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on

STN DUPLICATE 5

ACCESSION NUMBER: 1996:382822 BIOSIS
DOCUMENT NUMBER: PREV199699105178
TITLE: Formation of undifferentiated mesenteric tumors in transgenic mice expressing human neurotropic polyomavirus **early protein**.
AUTHOR(S): Franks, Roberta R.; Rencic, Adrienne; Gordon, Jennifer; Zoltick, Philip W.; Curtis, Mark; Knobler, Robert L.; Khalili, Kamel [Reprint author]
CORPORATE SOURCE: Molecular Neurovirology Sect., Jefferson Inst. Molecular Med., Dep. Biochem. Molecular Biol., Thomas Jefferson Univ., Philadelphia, PA 19107, USA
SOURCE: Oncogene, (1996) Vol. 12, No. 12, pp. 2573-2578. CODEN: ONCNES. ISSN: 0950-9232.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Aug 1996
Last Updated on STN: 26 Aug 1996

AB The human polyomavirus, JCV, is the established etiologic agent of the human demyelinating disease, progressive multifocal leukoencephalopathy (PML) seen in immunosuppressed individuals. In PML patients, the **viral early protein**, which is produced exclusively in glial **cells** is responsible for initiation of the **viral** lytic cycle. The JCV **early protein**, T-antigen, has greater than 70% homology to the well characterized SV40 **early protein** which has established oncogenic properties. To investigate the role of JCV T-antigen in tumorigenesis, transgenic mice containing the **viral** early **genome** were produced. Of the four positive transgenic animals, one developed severe neurological abnormalities and succumbed to death at 3 weeks of age. Another animal died with no visible gross pathology and the cause of death was not **determined**. The remaining two founders developed massive, undifferentiated, solid mesenteric tumors with no obvious neurological symptoms. Results from histologic analysis demonstrated the presence of highly cellular, poorly differentiated neoplastic **cells** in the tumor tissue. Electron microscopic evaluation of the tumor revealed the presence of a small blue **cell**-like tumor of epithelial/neuroectodermal origin. Results from RNA analysis by non-quantitative and highly sensitive RT-PCR indicated the presence of the JCV early transcript in various tissues, including **kidney**, liver, spleen, heart, lung, and brain, as well as in the tumors. However, analysis of the **viral early protein** by Western blot and immunohistochemistry indicated high level production of JCV **early protein** in the tumor tissue, but not in any other tissues. These observations present the first evidence for the development of inheritable neuroectodermal tumors induced by the human polyomavirus, JCV, **early protein** in a whole animal system.

L28 ANSWER 18 OF 46 MEDLINE on STN
ACCESSION NUMBER: 96190583 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8627705
TITLE: Phenotypic properties of **herpes** simplex **virus** 1 containing a derepressed open reading frame P gene.
AUTHOR: Lagunoff M; Randall G; Roizman B

Searcher : Shears 571-272-2528

CORPORATE SOURCE: Marjorie B. Kovler Viral Oncology Laboratories, University of Chicago, Illinois 60637, USA.
CONTRACT NUMBER: AI124009 (NIAID)
CA47451 (NCI)
SOURCE: Journal of virology, (1996 Mar) 70 (3) 1810-7.
Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960708
Last Updated on STN: 19970203
Entered Medline: 19960627

AB Open reading frame P (ORF P) maps in the **viral DNA** sequences transcribed during latency and is located antisense to the gamma 1 34.5 gene. Earlier studies have shown that the expression of ORF P is repressed by an infected cell protein number 4 binding site straddling the transcription initiation site. We have made monospecific polyclonal antibodies to the protein and constructed a **virus**, designated ORF P++, in which the infected cell protein number 4 binding site has been mutagenized, thereby allowing full expression of an unmodified ORF P gene from its natural promoter. We report the following findings. (i) The native protein forms multiple bands on denaturing polyacrylamide gels suggestive of extensive processing and aggregation of the protein; (ii) the protein accumulates in the nucleus in rod-shaped structures perpendicular to the axis of attachment of the infected **cell** to the solid matrix; (iii) the **virus** was highly attenuated on inoculation into mice by the intracerebral or **ocular** route, and **virus** was not recovered upon explantation of trigeminal ganglia; (iv) although protein synthesis was not prematurely shut off in the **human** neuroblastoma **cell** line SK-N-SH, gamma 1 34.5 protein was not **detected** in immunoblasts. Analyses of electrophoretically separated denatured RNAs indicated that in cells infected with the ORF P++ **virus**, there was a large increase in the amount of ORF P RNA and a corresponding decrease in the amount of gamma 1 34.5 RNA. We conclude that either the overproduction of ORF P protein blocks the expression of some **herpes** simplex **virus** 1 genes or derepression of the transcription of ORF P has a negative effect on the transcription of the antisense gamma 1 34.5 RNA.

L28 ANSWER 19 OF 46 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN

ACCESSION NUMBER: 1996:235680 BIOSIS
DOCUMENT NUMBER: PREV199698799809
TITLE: Cytomegalovirus replication in **human retinal** pigment epithelial **cells**: Altered expression of **viral early proteins**.
AUTHOR(S): Detrick, Barbara [Reprint author]; Rhame, Jean; Wang, Yun; Nagineni, Chandrasekharam N.; Hooks, John J.
CORPORATE SOURCE: George Washington Med. Cent., Ross Hall, Room 502, 2300 Eye St. NW, Washington, DC 20037, USA
SOURCE: Investigative Ophthalmology and Visual Science, (1996) Vol. 37, No. 5, pp. 814-825.
CODEN: IOVSDA. ISSN: 0146-0404.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 28 May 1996
Last Updated on STN: 28 May 1996

AB Purpose: Cytomegalovirus (CMV) infections are frequent complications in patients who have undergone **kidney** and bone marrow transplant and in patients with acquired immune deficiency syndrome. The mechanism by which CMV is activated and replicated within the **retina** is unknown. The authors evaluated the ability of **human** CMV to initiate replication in **human retinal** pigment epithelial (RPE) **cells** and compared this system with CMV replication in **human** fibroblasts (HEL-299, MRC-5) and **human** amnion epithelial (WISH) **cells**. Methods: **Human** RPE **cells** were obtained from donor **eyes** and propagated in vitro. Cells were infected, and CMV replication was evaluated in three ways: the **detection** of **viral** antigen by immunofluorescent, flow cytometry, and Western blot assays; the **detection** of **virus**-induced cytopathic effect (cpe), and the **detection** of infectious **virus**. Results: No evidence of **viral** replication in the epithelial (WISH) cells was found. Although CMV does not usually replicate in vitro in epithelial cells, CMV replication was **detected** in RPE cells. There are a number of distinct differences in CMV replication in RPE **cells** compared to replication in **human** fibroblasts. **Virus** -induced cpe and the production of infectious **virus** by RPE cells were delayed when compared to **virus** infection in either HEL or MRC 5 cells. At a multiplicity of infection of 0.1 and 1, cpe and infectious **virus** yield reached maximum levels at days 4 to 5 in fibroblasts and at days 19 to 46 in RPE cells, respectively. Nevertheless, infectious **virus** produced by RPE cells (10-6.5 TCID-50/0.1 ml) significantly surpassed levels produced by HEL cells (10-5.5 TCID-50/0.1 ml). The permissive infection in RPE cells consisted of a prolonged period (5 to 6 days) of **virus** production in the absence of cytopathology. **Virus** protein expression evaluated by indirect immunofluorescence assays, Western blot analysis, and flow cytometry revealed a delay in **viral** protein expression in RPE cells compared to **viral** protein expression in fibroblasts. The pattern of **viral** protein evaluated by flow cytometry was noticeably different in the two cell types. At the middle phase of CMV replication in RPE cells, a low percentage of cells express immediate early (IE) protein at a time when a high percentage of the cells express early (E) proteins. This IE-1 protein is a stable protein found concurrently with E protein in fibroblasts. This difference in percentage of cells expressing specific CMV proteins is transient, that is, it does not remain apparent at 100% cpe. Conclusions: **Retinal** pigment epithelial cells appear to demonstrate a distinct pattern of CMV infection. The low frequency of expression of IE **viral** protein in RPE cells, the subsequent slow replication of CMV, and the altered expression of IE **viral** proteins may be critical variables that impact on their relationship to **viral** persistence and activation within the **retina**. Alterations in the IE gene product may indicate the existence of positive or negative nuclear transcription factors within infected RPE cells.

L28 ANSWER 20 OF 46 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 96181434 MEDLINE

DOCUMENT NUMBER: PubMed ID: 8603861
TITLE: Adenovirus-mediated gene transfer of ornithine aminotransferase in cultured human **retinal** pigment epithelium.
AUTHOR: Sullivan D M; Chung D C; Anglade E; Nussenblatt R B; Csaky K G
CORPORATE SOURCE: National Eye Institute, National Institutes of Health, Bethesda, MD 20895, USA.
SOURCE: Investigative ophthalmology & visual science, (1996 Apr) 37 (5) 766-74.
Journal code: 7703701. ISSN: 0146-0404.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199605
ENTRY DATE: Entered STN: 19960524
Last Updated on STN: 19980206
Entered Medline: 19960516

AB PURPOSE: To evaluate the efficacy of adenovirus mediated transfer of ornithine delta-aminotransferase (OAT) into **human** **retinal** pigment epithelial (RPE) **cells**. METHODS: Adenovirus-mediated gene transfer into primary cultures of **human** RPE was evaluated by measurement of enzyme activity in whole **cell** extracts and by Western blot analysis. To assess mitochondrial integrity, succinate dehydrogenase activity was measured in transduced RPE cells. Expression of **adenovirus early** genes was evaluated using reverse transcription-polymerase chain reaction. RESULTS: OAT activity, which was 65 nmol/mg.hour in untransduced cells, could be increased to levels in excess of 20,000 nmol/mg.hour using an adenovirus vector carrying the OAT cDNA. There was, however, a significant reduction in succinate dehydrogenase activity associated with OAT activity greater than 12,000 nmol/mg.hour. Transduced human RPE displayed an altered morphology that appears to be a response to the vector because similar changes could be induced by an adenovirus vector that does not carry the OAT cDNA. **Adenovirus early** gene expression was **detected** in transduced RPE. CONCLUSIONS: This study represents a first step in the development of intraocular gene replacement therapy for the treatment of gyrate atrophy. The authors demonstrate that adenovirus is an efficient vehicle for the delivery of OAT into human RPE and that RPE will tolerate greater than a 150-fold increase in OAT-specific activity. Evidence for disruption of mitochondria when OAT activity exceeds 12,000 nmol/mg.hour and vector-induced toxicity indicate that more controlled transgene expression and refinement of the vector systems is needed.

L28 ANSWER 21 OF 46 MEDLINE on STN
ACCESSION NUMBER: 96275936 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8763171
TITLE: Imaging of RNA in situ hybridization by atomic force microscopy.
AUTHOR: Kalle W H; Macville M V; van de Corput M P; de Grooth B G; Tanke H J; Raap A K
CORPORATE SOURCE: Department of Cytochemistry and Cytometry, Leiden University, The Netherlands.
SOURCE: Journal of microscopy, (1996 Jun) 182 (Pt 3) 192-9.

Journal code: 0204522. ISSN: 0022-2720.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 19961015
Last Updated on STN: 19970203
Entered Medline: 19961002

AB In this study we investigated the possibility of imaging internal cellular molecules after cytochemical **detection** with atomic force microscopy (AFM). To this end, rat 9G and HeLa **cells** were hybridized with haptenized probes for 28S ribosomal RNA, **human** elongation factor mRNA and cytomegalovirus immediate early antigen mRNA. The haptenized hybrids were subsequently **detected** with a peroxidase-labelled antibody and visualized with 3.3'-diaminobenzidine (DAB). The influence of various scanning conditions on cell morphology and visibility of the signal was investigated. In order to **determine** the influence of ethanol dehydration on cellular structure and visibility of the DAB precipitate, cells were kept in phosphate-buffered saline (PBS) and scanned under fluid after DAB development or dehydrated and subsequently scanned dry or submerged in PBS. Direct information on the increase in height of cellular structures because of internally precipitated DAB and the height of mock-hybridized cells was available. Results show that internal DAB precipitate can be **detected** by AFM, with the highest sensitivity in the case of dry cells. Although a relatively large amount of DAB had to be precipitated inside the cell before it was visible by AFM, the resolution of AFM for imaging of RNA--in situ hybridization signals was slightly better than that of conventional **optical** microscopy. Furthermore, it is concluded that dehydration of the cells has irreversible effects on cellular structure. Therefore, scanning under fluid of previously dehydrated samples cannot be considered as a good representation of the situation before dehydration.

L28 ANSWER 22 OF 46 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 96079044 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7494307
TITLE: Neurons differentially control expression of a **herpes** simplex **virus** type 1 immediate-early promoter in transgenic mice.
AUTHOR: Mitchell W J
CORPORATE SOURCE: Laboratory of Experimental Neuropathology, National Institute of Neurological Disorders and Stroke, Bethesda, Maryland 20892, USA.
SOURCE: Journal of virology, (1995 Dec) 69 (12) 7942-50.
Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199601
ENTRY DATE: Entered STN: 19960217
Last Updated on STN: 19960217
Entered Medline: 19960111

AB The immediate-**early proteins** of **herpes**

simplex **virus** control the cascade of **viral** gene expression during lytic infection. It is not known which **viral** or host proteins control the reactivation of the **viral** **genome** in latently infected neurons. To **determine** whether neuronal proteins can regulate a **herpes** simplex **virus** immediate-early promoter in vivo, transgenic mice containing the promoter regulatory region of the **herpes** simplex **virus** type 1 immediate-early gene (ICP4) fused to the bacterial beta-galactosidase gene were generated. Two lines of mice, in the absence of **viral** proteins, displayed ICP4 promoter activity in neurons in specific locations in the central nervous system. The anatomic locations of these neurons were the hippocampus, cerebellar cortex, superior colliculus, indusium griseum, mammillary nucleus, cerebral cortex, and the dorsal laminae of the dorsal horns of the spinal cord. Additional subsets of neurons expressed the ICP4 promoter at lower levels; these included trigeminal ganglia and **retinas**. In a third line of mice, lower levels of expression were present in many of the above-described neurons. Many types of neurons, nearly all nonneuronal **cells** in the central nervous system, and some non-nervous system tissues were negative. **Viral** proteins including VP16 are not necessary to induce transcription from the ICP4 promoter in many neurons and some other **cell** types but may be required in most **cells** in vivo. An approximately 100-fold-greater number of neurons in the trigeminal ganglia expressed ICP4 promoter activity in newborn mice compared with adults. These data provide direct evidence that host proteins are sufficient to activate a **herpes** simplex **virus** immediate-early promoter in neurons in vivo and that a differential expression pattern for this promoter exists within different neuronal phenotypes and between the same neurons in different ages of mice.

L28 ANSWER 23 OF 46 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 94236346 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8180775
TITLE: A comparative study of congenital and postnatally acquired human cytomegalovirus infection in infants: lack of expression of **viral** immediate **early** **protein** in congenital cases.
AUTHOR: Maeda A; Sata T; Sato Y; Kurata T
CORPORATE SOURCE: Department of Pathology, National Institute of Health, Tokyo, Japan.
SOURCE: Virchows Archiv : an international journal of pathology, (1994) 424 (2) 121-8.
Journal code: 9423843. ISSN: 0945-6317.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199406
ENTRY DATE: Entered STN: 19940621
Last Updated on STN: 19950307
Entered Medline: 19940616

AB Postmortem tissues from infants with congenital and postnatally acquired human cytomegalovirus (HCMV) infection were examined by routine histology, immunohistochemistry (IHC) and in situ hybridization (ISH) to **determine** the dynamics of **viral** replication in vivo.

Histologically, infants in both groups showed characteristic inclusion-bearing **cells** most commonly in lung, **kidney**, liver and pancreas. IHC for late proteins using a rabbit polyclonal antibody and ISH for **viral genomes detected** most of the infected **cells** as nuclear and/or cytoplasmic signals. However, immunostaining with a monoclonal antibody against **viral** immediate early (IE) proteins was variable depending on the stage of **viral** replication within an individual infected **cell**. In tissues of infants with postnatal HCMV infection, many **cells** harboured IE antigens, while in tissues from congenital cases most of the affected **cells** lacked IE antigens and only a few showed cytoplasmic staining. The difference was not caused by the antigenic diversity among **viral** strains as confirmed by in vitro study. Our findings suggested that congenital infections exhibited uniformly late stage proteins with inactive **viral** replication at death, while acquired ones remained active. The different **viral** activity may reflect the immune status of congenital and acquired HCMV infections.

L28 ANSWER 24 OF 46 MEDLINE on STN
ACCESSION NUMBER: 90218026 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2139107
TITLE: Definition of adenovirus type 5 functions involved in the induction of chromosomal aberrations in **human cells**.
AUTHOR: Caporossi D; Bacchetti S
CORPORATE SOURCE: Department of Pathology, McMaster University, Hamilton, Ontario, Canada.
SOURCE: Journal of general virology, (1990 Apr) 71 (Pt 4) 801-8. Journal code: 0077340. ISSN: 0022-1317.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199005
ENTRY DATE: Entered STN: 19900622
Last Updated on STN: 19900622
Entered Medline: 19900521

AB Infection of **human** embryonic **kidney cells** with adenovirus type 5 (Ad5) induces aberrations (gaps and breaks) in the **cell** chromosomes. We have conducted a study utilizing a large number of Ad5 mutants to identify the **viral** functions that are responsible for the occurrence of cytogenetic damage. The results of our investigation have indicated that expression of the gene products of the Ad5 early region 1A (E1A) is necessary for the induction of chromosomal aberrations and that other early **viral** gene products do not appear to contribute to this phenotype. We have also shown that expression of both the major E1A gene products, the 243 amino acid and the 289 amino acid proteins, is required for induction of damage at wild-type levels, although the 289 amino acid protein appears to retain **detectable** activity on its own. Lastly, we have observed that deletions in the amino-terminal region of the E1A proteins and in the transactivating domain of the 289 amino acid protein prevent the occurrence of cytogenetic damage, whereas mutations elsewhere in the proteins do not affect this process.

L28 ANSWER 25 OF 46 MEDLINE on STN
ACCESSION NUMBER: 90320132 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2142558
TITLE: Transactivation of the p53 oncogene by E1a gene products.
AUTHOR: Braithwaite A; Nelson C; Skulimowski A; McGovern J; Pigott D; Jenkins J
CORPORATE SOURCE: Division of Cell Biology, John Curtin School of Medical Research, Australian National University, Canberra.
SOURCE: Virology, (1990 Aug) 177 (2) 595-605.
Journal code: 0110674. ISSN: 0042-6822.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199008
ENTRY DATE: Entered STN: 19900921
Last Updated on STN: 19900921
Entered Medline: 19900821

AB Infection of quiescent rat **kidney cells** with **human** adenovirus is shown to transcriptionally stimulate (transactivate) the p53 oncogene. The increased transcription results in an accumulation of p53-specific mRNA in parallel with an increase in p53 protein levels, although there is a considerable delay between transcriptional activation and the **detection** of stable p53 mRNA and protein. The induction of p53 is **detectable** with two monoclonal antibodies recognizing different epitopes. The induction of p53 by adenovirus is delayed compared to induction by serum, and it occurs after the onset of adenovirus-induced cellular **DNA** replication. Thus, adenovirus-induced **DNA** replication bypasses a G0/G1 control point. Experiments with hydroxyurea show that p53 activation does not require continued cell cycling and thus is likely to be a direct consequence of **viral** gene expression. Finally, the induction of p53 is shown to be dependent on expression of the 289-residue product encoded by the **viral** E1a gene.

L28 ANSWER 26 OF 46 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 90188303 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2138209
TITLE: Adenovirus type 12 tumour antigen synthesis differs during infection of permissive and non-permissive cells.
AUTHOR: Lucher L A
CORPORATE SOURCE: Department of Biological Sciences, Illinois State University, Normal 61761.
CONTRACT NUMBER: 1-R15-AI24094-01A1 (NIAID)
SOURCE: Journal of general virology, (1990 Mar) 71 (Pt 3) 579-83.
Journal code: 0077340. ISSN: 0022-1317.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199004
ENTRY DATE: Entered STN: 19900601
Last Updated on STN: 19970203
Entered Medline: 19900423

AB Synthesis of the adenovirus type 12 E1A and E1B tumour antigens was compared in productively infected **human** (KB) **cells** and

in abortively infected baby hamster **kidney** (BHK) **cells** . By the use of anti-peptide antibodies, the E1A tumour antigens were easily **detectable** in infected KB extracts as early as 6 h post-infection, but were not **detectable** in infected BHK extracts until 12 h post-infection. The level of E1A tumour antigens **detected** in BHK extracts was 10 to 15% of that **detected** in KB extracts. The level of the E1B 163R (19K) tumour antigen was also lower in BHK extracts: 5 to 10% of that **detected** in KB extracts. Stability of the E1A tumour antigens was not significantly different in the two infected cell species, indicating that the lower E1A level during abortive infection was due to a lower rate of synthesis of these proteins. These data suggest that **early protein** synthesis is not the same in abortively infected cells as it is in productively infected cells.

L28 ANSWER 27 OF 46 MEDLINE on STN
ACCESSION NUMBER: 89146137 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2521957
TITLE: Point mutational inactivation of the retinoblastoma antioncogene.
AUTHOR: Horowitz J M; Yandell D W; Park S H; Canning S; Whyte P; Buchkovich K; Harlow E; Weinberg R A; Dryja T P
CORPORATE SOURCE: Whitehead Institute for Biomedical Research, Massachusetts Institute of Technology, Cambridge 02142.
CONTRACT NUMBER: CA 08131 (NCI)
CA 13106 (NCI)
CA 39826 (NCI)
+
SOURCE: Science, (1989 Feb 17) 243 (4893) 937-40.
Journal code: 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198903
ENTRY DATE: Entered STN: 19900306
Last Updated on STN: 19970203
Entered Medline: 19890328

AB The retinoblastoma (Rb) antioncogene encodes a nuclear phosphoprotein, p105-Rb, that forms protein complexes with the adenovirus E1A and SV40 large T oncoproteins. A novel, aberrant Rb protein **detected** in J82 bladder carcinoma **cells** was not able to form a complex with E1A and was less stable than p105-Rb. By means of a rapid method for the **detection** of mutations in Rb mRNA, this defective Rb protein was observed to result from a single point mutation within a splice acceptor sequence in J82 **genomic DNA**. This mutation eliminates a single exon and 35 amino acids from its encoded protein product.

L28 ANSWER 28 OF 46 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 88337370 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2844011
TITLE: **Human** cytomegalovirus infection of **kidney** glomerular visceral epithelial and tubular epithelial **cells** in culture.
AUTHOR: Heieren M H; Kim Y K; Balfour H H Jr
CORPORATE SOURCE: Department of Laboratory Medicine and Pathology, University

of Minnesota, Minneapolis 55455.
CONTRACT NUMBER: AI10704 (NIAID)
AM13083 (NIADDK)
AM25518 (NIADDK)
SOURCE: Transplantation, (1988 Sep) 46 (3) 426-32.
Journal code: 0132144. ISSN: 0041-1337.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198810
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19881026

AB Evidence suggests that human cytomegalovirus is resident in the **kidneys** of seropositive donors at the time of transplantation, and CMV has been implicated in both glomerulonephritis and interstitial nephritis. In this study we assessed the interactions of CMV with two **human renal cell** types in culture: glomerular visceral epithelial **cells** (GVE) and **renal** tubular epithelial (RTE) **cells**. GVE permitted **viral** adsorption, penetration, nuclear translocation, and restricted **viral** transcription. However, early **viral** protein expression was not **detectable** by immunofluorescence and infectious virions were not produced. In contrast, retinoic acid-treated GVE permitted early **viral** protein expression and supported CMV replication. RTE also permitted **viral** adsorption and penetration. CMV-specific **early proteins** were readily observed by immunofluorescence, and CMV **DNA** replication was observed by **DNA** dot blot hybridization. Assays comparing **viral** yield with **viral DNA** synthesis indicated that RTE were capable of supporting persistent and prolonged **viral** expression without significant cell death for at least 55 days after infection. We believe that these findings should explain chronic viruria in individuals with symptomatic and asymptomatic CMV infection. In addition, GVE could also be a potential source of CMV transmission when altered by disease or transplantation.

L28 ANSWER 29 OF 46 MEDLINE on STN
ACCESSION NUMBER: 88062977 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2824843
TITLE: Regulation of glycoprotein D synthesis: does alpha 4, the major regulatory protein of **herpes** simplex **virus** 1, regulate late genes both positively and negatively?.
AUTHOR: Arsenakis M; Campadelli-Fiume G; Roizman B
CORPORATE SOURCE: Marjorie B. Kovler Viral Oncology Laboratories, University of Chicago, Illinois 60637.
CONTRACT NUMBER: CA 08494 (NCI)
CA 19264 (NCI)
SOURCE: Journal of virology, (1988 Jan) 62 (1) 148-58.
Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 198801
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19970203
Entered Medline: 19880121

AB Earlier studies have described the alpha 4/c113 baby hamster **kidney cell** line which constitutively expresses the alpha 4 protein, the major regulatory protein of **herpes** simplex **virus** 1 (**HSV**-1). Introduction of the HSV-1 glycoprotein B (gB) gene, regulated as a gamma 1 gene, into these **cells** yielded a **cell** line which constitutively expressed both the alpha 4 and gamma 1 gB genes. The expression of the gB gene was dependent on the presence of functional alpha 4 protein. In this article we report that we introduced into the alpha 4/c113 and into the parental BHK **cells**, the HSV-1 BamHI J fragment, which encodes the domains of four genes, including those of glycoproteins D, G, and I (gD, gG, and gI), and most of the coding sequences of the glycoprotein E (gE) gene. In contrast to the earlier studies, we obtained significant constitutive expression of gD (also a gamma 1 gene) in a **cell** line (BJ) derived from parental BHK **cells**, but not in a **cell** line (alpha 4/BJ) which expresses functional alpha 4 protein. RNA homologous to the gD gene was present in significant amounts in the BJ **cell** line; smaller amounts of this RNA were **detected** in the alpha 4/BJ **cell** line. RNA homologous to gE, presumed to be polyadenylated from signals in the vector sequences, was present in the BJ **cells** but not in the alpha 4/BJ **cells**. The expression of the HSV-1 gD and gE genes was readily induced in the alpha 4/BJ **cells** by superinfection with HSV-2. The BJ **cell** line was, in contrast, resistant to expression of HSV-1 and HSV-2 genes. The BamHI J **DNA** fragment copy number was approximately 1 per BJ **cell genome** equivalent and 30 to 50 per alpha 4/BJ **cell genome** equivalent. We conclude that (i) the genes specifying gD and gB belong to different **viral** regulatory gene subsets, (ii) the gD gene is subject to both positive and negative regulation, (iii) both gD and gE mRNAs are subject to translational controls although they may be different, and (iv) the absence of expression of gD in the alpha 4/BJ **cells** reflects the expression of the alpha 4 protein in these **cells**.

L28 ANSWER 30 OF 46 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 1987:44186 BIOSIS
DOCUMENT NUMBER: PREV198783023532; BA83:23532
TITLE: ACTIVATION OF THE ADENOVIRUS AND BK **VIRUS** LATE PROMOTERS EFFECTS OF THE BK **VIRUS** ENHANCER AND TRANS-ACTING **VIRAL EARLY PROTEINS**.
AUTHOR(S): GRINNELL B W [Reprint author]; BERG D T; WALLS J
CORPORATE SOURCE: DEP MOLECULAR BIOLOGY, LILLY RESEARCH LAB, LILLY CORPORATE CENTER, INDIANAPOLIS, INDIANA 46285, USA
SOURCE: Molecular and Cellular Biology, (1986) Vol. 6, No. 11, pp. 3596-3605.
CODEN: MCEBD4. ISSN: 0270-7306.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 7 Jan 1987

Searcher : Shears 571-272-2528

Last Updated on STN: 7 Jan 1987

AB We have examined the activation of the adenovirus major late promoter (MLP) by the cis-acting enhancer element of the human polyomavirus BK and by the trans-acting simian **virus** 40 (SV40) T antigen and adenovirus E1A proteins. By using chloramphenicol acetyltransferase expression vectors, we found that the MLP (pLP-CAT) was trans-activated in **human** and monkey **kidney cells** expressing the SV40 T antigen. In addition, the MLP could be cis-activated by the BK **virus** enhancer in both **human** and monkey **kidney cells**; approximately 20 times more chloramphenicol acetyltransferase was produced from expression vectors containing the MLP alone. This same level of enhancement of the MLP by the BK enhancer was observed in cells expressing the T antigen of SV40. However, in the 293 cell line, greater enhancement of MLP activity (70-fold) was observed with the BK enhancer sequence. In contrast, MLP activity in the 293 cell line was unchanged by the SV40 enhancer. In contransfection experiments, MLP activity, augmented by the BK enhancer, could be further stimulated with a plasmid coding for the E1A gene products. By creating deletion mutants, we **determined** that the high-level activation of the hybrid BL transcriptional unit by the E1A proteins requires both MLP sequences and an intact BK **virus** enhancer. On the other hand, activation of the BL transcriptional unit by the T antigen did not require an intact enhancer sequence. Our results suggest that the SV40 T antigen and E1A proteins trans-activate the BL promoter by different mechanisms. We also demonstrate in cotransfection experiments that the BK late promoter is activated 45-fold by the SV40 T antigen.

L28 ANSWER 31 OF 46 MEDLINE on STN
ACCESSION NUMBER: 86144054 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2936899
TITLE: The adenovirus type 12 early-region 1B 58,000-Mr gene product is required for **viral DNA** synthesis and for initiation of cell transformation.
AUTHOR: Shiroki K; Ohshima K; Fukui Y; Ariga H
SOURCE: Journal of virology, (1986 Mar) 57 (3) 792-801. Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198603
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19900321
Entered Medline: 19860328

AB An E1B 58K mutant of adenovirus type 12 (Ad12), dl207, was constructed by the deletion of 852 base pairs in the E1B 58K coding region. The mutant could grow efficiently in 293E1 **cells** but not in HeLa, KB, or **human** embryo **kidney** (HEK) **cells**. **Viral DNA** replication of dl207 was not **detected** in HeLa and KB cells and was seldom **detected** in HEK cells. Analysis of **viral DNA** synthesis in vitro showed that the Ad12-**DNA**-protein complex replicated by using the nuclear extract from Ad12 wild-type (WT)-infected HeLa cells but not by using the nuclear extract from dl207-infected cells. In dl207-infected HeLa and KB cells, early mRNAs were **detected**, but late mRNAs were not **detected**. The mutant induced fewer transformed foci than the WT

in rat 3Y1 cells. Cells transformed by dl207 could grow efficiently in fluid medium, form colonies in soft agar culture, and induce tumors in rats transplanted with the transformed cells at the same efficiency as WT-transformed cells. Tumors were induced in hamsters injected with WT virions but were not induced in hamsters injected with dl207 virions. The results indicate that the E1B 58K protein is required both for **viral DNA** replication in productive infection and for initiation of cell transformation, but not for maintenance of the transformed phenotype.

L28 ANSWER 32 OF 46 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 85211028 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2987529
TITLE: **DNA** rearrangement in the control region for early transcription in a **human** polyomavirus JC host range mutant capable of growing in **human** embryonic **kidney cells.**
AUTHOR: Miyamura T; Furuno A; Yoshiike K
SOURCE: Journal of virology, (1985 Jun) 54 (3) 750-6. Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-J02226; GENBANK-J02227; GENBANK-K02561; GENBANK-V01118
ENTRY MONTH: 198507
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19900320
Entered Medline: 19850702

AB A **human** polyomavirus JC **virus** (JCV) host range mutant (JC-HEK) can grow in **human** embryonic **kidney cells**, whereas the brain **cell**-tropic wild-type JCV strain (Mad-1) cannot; JC-HEK contains two complementing defective **DNAs**, JC-HEK-A and JC-HEK-B. We **determined** the nucleotide sequence of the putative transcriptional control region of JC-HEK-A **DNA** that can induce T-antigen synthesis in **human** embryonic **kidney cells** and compared it with the sequence of JCV Mad-1 **DNA**. The JC-HEK-A control region was found to have a complex **DNA** rearrangement, namely, a partial local duplication of a noncoding region generating two extra replication origins and translocation of segments from the large-T-antigen gene (415 base pairs) and the VP-1 gene (78 base pairs). In the rearranged segment, JC-HEK-A had seven sets of the sequence 5'TGGA(T)A(T)A(T)3', which is found in the simian **virus** 40 enhancer core, whereas JCV Mad-1 had only one set in its control region. JC-HEK-A also had a 5'TGGAAGTGTAA3' sequence resembling the **adenovirus early** region 1A enhancer core sequence 5'AGGAAGTGAA3'. Because the **viral** enhancer is host discriminatory and because another **human** polyomavirus, BK **virus**, that grows well in **human** embryonic **kidney cells** has these signals in its control region, it is likely that some of the newly acquired signals in JC-HEK play an important role in the altered host range of JCV.

L28 ANSWER 33 OF 46 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN

ACCESSION NUMBER: 1984:290582 BIOSIS
DOCUMENT NUMBER: PREV198478027062; BA78:27062
TITLE: **ADENOVIRUS EARLY** REGION 1A PROTEIN ACTIVATES TRANSCRIPTION OF A NONVIRAL GENE INTRODUCED INTO MAMMALIAN CELLS BY INFECTION OR TRANSFECTION.
AUTHOR(S): GAYNOR R B [Reprint author]; HILLMAN D; BERK A J
CORPORATE SOURCE: DEP MED, SCH MED, UNIV CALIF, LOS ANGELES, CA 90024, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1984) Vol. 81, No. 4, pp. 1193-1197.
CODEN: PNASA6. ISSN: 0027-8424.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB Transcription from all early adenovirus promoters is stimulated by a 289 amino acid phosphoprotein encoded in the pre-early transcription unit E1A. To **determine** if this protein could act on a nonviral gene placed on the **viral** chromosome, adenovirus recombinants were constructed in which the rat preproinsulin I gene, including its promoter region, was substituted in both orientations for E1A. Preproinsulin mRNA synthesis from these recombinants was greatly stimulated after infection of line 293 **human** embryonic **kidney cells**, which constitutively express E1A protein, compared to **human** cervical carcinoma HeLa **cells**, which do not. Expression of the preproinsulin gene was also greatly stimulated when HeLa cells were coinfected with the recombinants and wild-type adenovirus or a mutant defective in a 2nd E1A protein, but much less so by coinfection with a mutant defective in the 289 amino acid phosphoprotein. Much of the E1A-induced preproinsulin mRNA had a 5' end at the same position as the preproinsulin mRNA isolated from insulinoma cells, but a considerable fraction had 5' ends mapping heterogeneously within several hundred nucleotides of this site. Preproinsulin mRNA was also **detected** in 293 **cells** but not HeLa or **human** embryonic **kidney** HEK **cells** after transfection of a plasmid containing the preproinsulin gene with no adenovirus sequence. This indicates that there is no cis-acting adenovirus sequence required for E1A protein stimulation of preproinsulin transcription. Infection of rat cells with adenovirus did not induce **detectable** mRNA synthesis from the endogenous preproinsulin I gene. These results demonstrate that the E1A protein can induce expression of a nonviral gene when it is newly introduced into mammalian cells by **viral** infection or transfection, but it does not induce the endogenous cellular gene.

L28 ANSWER 34 OF 46 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 1984:298588 BIOSIS
DOCUMENT NUMBER: PREV198478035068; BA78:35068
TITLE: ADENOVIRUS 2 EARLY REGION 1A STIMULATES EXPRESSION OF **VIRAL** AND CELLULAR GENES.
AUTHOR(S): SVENSSON C [Reprint author]; AKUSJARVI G
CORPORATE SOURCE: DEP MED GENET, UPPSALA UNIV, BIOMED CENT, BOX 589, S-751 23 UPPSALA, SWEDEN
SOURCE: EMBO (European Molecular Biology Organization) Journal, (1984) Vol. 3, No. 4, pp. 789-794.
CODEN: EMJODG. ISSN: 0261-4189.
DOCUMENT TYPE: Article

FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB The ability of products from the **adenovirus early** region 1A to stimulate **viral** and cellular gene expression has been studied, using a transient expression assay in **human** cervical carcinoma HeLa **cells**. The E1A 13S mRNA encodes a diffusible product which is capable of stimulating transcription of adenovirus genes and the rabbit β-globin gene. The E1A 12S mRNA has no **detectable** stimulatory effect on either cellular or **viral** genes. Although being able to stimulate both types of genes, the E1A regulatory protein enhances **viral** gene expression .apprx. 10 times more than β-globin gene expression. When connected to the cis-acting SV40 enhancer element, the β-globin gene cannot be further stimulated by the trans-acting E1A product. Transfection of either adenovirus or the β-globin gene into **human** embryonic **kidney** 293 **cells**, which constitutively expresses the E1A gene products, leads to an enhanced expression which is 10- to 20-fold higher than obtained by co-transfection of HeLa **cells**. The 293 cells thus provide a simple assay to demonstrate E1A-mediated transcriptional regulation.

L28 ANSWER 35 OF 46 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 1984:287626 BIOSIS
DOCUMENT NUMBER: PREV198478024106; BA78:24106
TITLE: **ADENOVIRUS EARLY** REGION 1B 58000 DALTON TUMOR ANTIGEN IS PHYSICALLY ASSOCIATED WITH AN EARLY REGION 4 25000 DALTON PROTEIN IN PRODUCTIVELY INFECTED **CELLS**.
AUTHOR(S): SARNOW P [Reprint author]; HEARING P; ANDERSON C W; HALBERT D N; SHENK T; LEVINE A J
CORPORATE SOURCE: DEP MICROBIOL, SCH MED, STATE UNIV NY STONY BROOK, STONY BROOK, NY 11794, USA
SOURCE: Journal of Virology, (1984) Vol. 49, No. 3, pp. 692-700. CODEN: JOVIAM. ISSN: 0022-538X.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB In soluble protein extracts obtained from adenovirus productive infected **cells**, monoclonal antibodies directed against the early region 1B 58,000-dalton (E1B-58K) protein immunoprecipitated, in addition to this protein, a polypeptide of 25,000 MW. An analysis of tryptic peptides derived from this 25K protein demonstrated that it was unrelated to the E1B-58K protein. The tryptic peptide maps of the 25K protein produced in adenovirus 5 (Ad5)-infected **human** cervical carcinoma HeLa **cells** and hamster **kidney** BHK **cells** were identical; Ad3-infected HeLa **cells** produced a different 25K protein. The **viral** origin of this 25K protein was confirmed by an amino acid sequence **determination** of 5 methionine residues in 2 Ad2 tryptic peptides derived from the 25K protein. The positions of these methionine residues in the 25K protein were compared with the nucleotide sequence of Ad2 and uniquely mapped the gene for this protein to early region 4, subregion 6 of the **viral genome**. A mutant of Ad5 was obtained (Ad5 d1342) which failed to produce **detectable** levels of the E1B-58K protein. In HeLa **cells** infected with this mutant, monoclonal antibodies directed against the

E1B-58K protein failed to **detect** the associated 25K protein. In **human** embryonic **kidney** 293 **cells** infected with Ad5 dl342, which contain an E1B/58K protein encoded by the integrated adenovirus **genome**, the mutant produced an E4-25K protein which associated with the E1B-58K protein derived from the integrated **genome**. Extracts of labeled Ad5 dl342-infected HeLa **cells** or 293 **cells** (E1B-58K+). When the mixed extracts were incubated with the E1B-58K monoclonal antibody, a labeled E4-25K protein was coimmunoprecipitated. When extracts of Ad5 dl342-infected HeLa **cells** and uninfected HeLa **cells** (both E1B-58K-) were mixed, the E1B-58K monoclonal antibody failed to immunoselect the E4-25K protein. Evidently, the E1B-58K antigen is physically associated with an E4-25K protein in productively infected **cells**. This is the same E1B-58K protein that was previously shown to be associated with the cellular p53 antigen in adenovirus-transformed **cells**.

L28 ANSWER 36 OF 46 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN

ACCESSION NUMBER: 1984:330552 BIOSIS
DOCUMENT NUMBER: PREV198478067032; BA78:67032
TITLE: CONSTRUCTION AND FUNCTIONAL CHARACTERIZATION OF POLYOMA **VIRUS GENOMES** THAT SEPARATELY ENCODE THE 3 **EARLY PROTEINS**.
AUTHOR(S): ZHU Z [Reprint author]; VELDMAN G M; COWIE A; CARR A; SCHAFFHAUSEN B; KAMEN R
CORPORATE SOURCE: GENETICS INSTITUTE, BOSTON, MA 02115, USA
SOURCE: Journal of Virology, (1984) Vol. 51, No. 1, pp. 170-180. CODEN: JOVIAM. ISSN: 0022-538X.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB Modified polyoma **virus genomes** that individually encode the large and small T proteins were constructed by exchanging restriction endonuclease fragments between c[complementary]**DNA** copies of the respective mRNA and cloned **genomic DNA**. The efficacies of the new constructs, and that of the middle T protein gene described previously, were demonstrated with SV40 polyoma **virus** early genes. Each of the 3 recombinant **viruses** induced the synthesis of only the expected polyoma **virus early protein** in infected African green monkey **kidney** CV-1 **cells**. The rates of synthesis of large, middle and small T proteins were .apprx. 1.5, 4.0 and 9.0 times the rate of synthesis of SV40 large T protein, respectively. The deletion of introns had no detrimental effect on mRNA biogenesis. A further polyoma **virus**-SV40 recombinant, containing wild-type polyoma **virus** early region **DNA**, expressed an aberrant 58,000-dalton form of the middle T protein which may result from utilization of a cryptic splice site. Immunofluorescence studied with monkey **cells** infected by the recombinant **viruses** allowed us to **determine** the cellular locations of the polyoma **virus early proteins**. Overproduction of the middle T protein did not result in a corresponding overproduction of the middle T protein-associated tyrosine phosphokinase activity.

L28 ANSWER 37 OF 46 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN

ACCESSION NUMBER: 1984:303709 BIOSIS
DOCUMENT NUMBER: PREV198478040189; BA78:40189
TITLE: RECOMBINATION BETWEEN SV-40 AND ADENO ASSOCIATED **VIRUS** VIRION CO INFECTION COMPARED TO **DNA** CO TRANSFECTION.
AUTHOR(S): GROSSMAN Z [Reprint author]; WINOCOUR E; BERNS K I
CORPORATE SOURCE: DEP IMMUNOLOGY MED MICROBIOLOGY, UNIV FLA COLLEGE MED, J HILLIS MILLER MED CENTER, BOX J-266, GAINESVILLE, FL 32610, USA
SOURCE: Virology, (1984) Vol. 134, No. 1, pp. 125-137. CODEN: VIRLAX. ISSN: 0042-6822.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB Recombination between SV40 and adeno-associated **virus** (AAV) was **detected**, by infectious center in situ plaque hybridization procedures, after both **DNA** cotransfection and virion coinfection of African green monkey **kidney** BSC-1 **cells**. The number of **cells** producing recombinants (1 in 1000) was the same, irrespective of the way in which the SV40 and AAV **genomes** were delivered to the **cell**, despite the fact that 5-10 times more **cells** were infected after virion coinfection. Several other dosage-response parameters of the recombination process consequent to virion coinfection were comparable to those after **DNA** cotransfection. The sole difference observed between the 2 infection systems was that the SV40/AAV recombinants formed after virion coinfection contained an inordinately high proportion of AAV terminal **DNA** sequences. By separating the SV40 and AAV infections in time, such that the AAV infection was delayed until after certain events in the SV40 cycle had taken place, an optimum phase for recombination in the SV40 cycle was identified. This phase occurs a few hours after infection, well before the onset of SV40 **DNA** replication and the synthesis of SV40-specific **early proteins**.

L28 ANSWER 38 OF 46 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 1984:258319 BIOSIS
DOCUMENT NUMBER: PREV198477091303; BA77:91303
TITLE: CHARACTERIZATION OF THE IMMEDIATE EARLY FUNCTIONS OF PSEUDORABIES **VIRUS**.
AUTHOR(S): IHARA S [Reprint author]; FELDMAN L; WATANABE S; BEN-PORAT T
CORPORATE SOURCE: DEP MICROBIOL, VANDERBILT UNIV, SCH MED, NASHVILLE, TENN 37232, USA
SOURCE: Virology, (1983) Vol. 131, No. 2, pp. 437-454. CODEN: VIRLAX. ISSN: 0042-6822.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB The immediate-early transcripts of pseudorabies **virus** have been located in a region of the **genome** situated internally within the inverted repeat between map positions 0.99 and 0.95. A single immediate-early transcript (.apprx. 6 kb [kilobases]) can be **detected** both in the cytoplasmic and nuclear fractions of infected, cycloheximide-treated [rabbit **kidney**] **cells**. Analysis of the proteins synthesized after removal of cycloheximide from

infected **cells** or after translation in vitro of the RNA isolated from these **cells** revealed the presence of a single protein (180K) not present in similarly treated, uninfected **cells**. That this is a **virus** protein and is specified by the immediate-early region of the **genome** was shown by selection and translation of mRNA hybridizing with **virus DNA** from the appropriate region of the **genome**. The effects of infection of **cells** with a temperature-sensitive mutant (tsG1) defective in the 180K protein were studied. At the nonpermissive temperature only immediate-early RNA was transcribed and only one **virus** protein, the 180K protein, was synthesized. Inhibition of cellular protein and **DNA** synthesis was also observed. After shift down of tsG1-infected **cells** from the nonpermissive to the permissive temperature at 3 h post-infection, a transition to early RNA transcription occurred. If the shift down was delayed until 5 h post-infection, transcription of the **virus genome** was completely inhibited and an abortive infection ensued. Shift up of the mutant-infected **cells** from the permissive to the nonpermissive temperature resulted in a decrease in the rate of accumulaton of early and late transcripts, and a resumption of the synthesis of immediate-early RNA and protein. From these as well as from previous results, it is concluded that pseudorabies **virus** codes for a single multifunctional immediate-**early protein** which is essential for the transition from the transcription of immediate-early to early RNA and is required for the continuous transcription of early (and late) RNA. The immediate-**early protein** is also self-regulatory; the presence of the functional immediate-**early protein** represses the transcription of its RNA. The immediate **early protein** of pseudorabies **virus** appears to play a direct role, under certain conditions, in the inhibition of cellular macromolecular synthesis.

L28 ANSWER 39 OF 46 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 82242296 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6284977
TITLE: Effect of deletions in **adenovirus early** region 1 genes upon replication of adeno-associated **virus**.
AUTHOR: Laughlin C A; Jones N; Carter B J
SOURCE: Journal of virology, (1982 Mar) 41 (3) 868-76.
Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198209
ENTRY DATE: Entered STN: 19900317
Last Updated on STN: 19970203
Entered Medline: 19820910

AB The growth of adeno-associated **virus** (AAV) is dependent upon helper functions provided by adenovirus. We investigated the role of **adenovirus early** gene region 1 in the AAV helper function by using six adenovirus type 5 (Ad5) host range mutants having deletions in early region 1. These mutants do not grow in **human** KB **cells** but are complemented by and grow in a line of adenovirus-transformed **human** embryonic **kidney**

cells (293 **cells**); 293 **cells** contain and express the Ad5 early region 1 genes. Mutants having extensive deletions of **adenovirus early** region 1a (dl312) or regions 1a and 1b (dl313) helped AAV as efficiently as wild-type adenovirus in 293 **cells**, but neither mutant helped in KB **cells**. No AAV **DNA**, RNA, or protein synthesis was **detected** in KB **cells** in the presence of the mutant adenoviruses. Quantitative blotting experiments showed that at 20 h after infection with AAV and either dl312 or dl313 there was less than one AAV **genome** per **cell**. In KB **cells** infected with AAV alone, the unreplicated AAV **genomes** were **detected** readily. Apparently, infection with adenovirus mutant dl312 or dl313 results in degradation of most of the infecting AAV **genomes**. We suggest that at least an adenovirus region 1b product (and perhaps a region 1a product also) is required for AAV **DNA** replication. This putative region 1b function appears to protect AAV **DNA** from degradation by an adenovirus-induced DNase. We also tested additional Ad5 mutants (dl311, dl314, sub315, and sub316). All of these mutants were inefficient helpers, and they showed varying degrees of multiplicity leakiness. dl312 and dl313 complemented each other for the AAV helper function, and each was complemented by Ad5ts125 at the nonpermissive temperature. The defect in region 1 mutants for AAV helper function acts at a different stage of the AAV growth cycle than the defect in the region 2 mutant ts125.

L28 ANSWER 40 OF 46 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN

ACCESSION NUMBER: 1983:211626 BIOSIS
DOCUMENT NUMBER: PREV198375061626; BA75:61626
TITLE: CHARACTERIZATION OF CYTOMEGALOVIRUS IMMEDIATE EARLY GENES 1. NONPERMISSIVE RODENT CELLS OVER PRODUCE THE IMMEDIATE EARLY IE-94K PROTEIN FROM CYTOMEGALOVIRUS COLBURN.
AUTHOR(S): JEANG K-T [Reprint author]; CHIN G; HAYWARD G S
CORPORATE SOURCE: DEP PHARMACOL EXP THERAPEUTICS, JOHNS HOPKINS UNIV SCH MED, 725 N WOLFE ST, BALTIMORE, MD 21205, USA
SOURCE: Virology, (1982) Vol. 121, No. 2, pp. 393-403. CODEN: VIRLAX. ISSN: 0042-6822.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB The Colburn strain of simian cytomegalovirus (CMV) gives high-yield productive infections in both **human** fibroblasts (HF) and African green monkey **kidney** Vero **cells** and in these **cells** a major immediate-**early protein** of 94K (IE94) has been identified in cycloheximide reversal experiments. In BALB/c-3T3 or Rat-1 cells infection with CMV (Colburn) does not yield infectious progeny virions or produce cytopathic effects and the **virus** fails to replicate its **DNA**. A single, **viral**-specific phosphorylated protein of MW 94K was overproduced in the nonproductive infections. No other **detectable viral** polypeptides were synthesized even at late times. Mouse antiserum elicited against this 94K protein in infected BALB/c-3T3 cells immunoprecipitated the IE94 protein from infected HF cells, demonstrating that the same immediate-early gene product is expressed in both permissive and nonpermissive cells. Evidently, the amplified expression of this immediate-early gene in rodent cells can be explained by increased

reutilization of stabilized 94K specific mRNA as opposed to increased transcription.

L28 ANSWER 41 OF 46 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 1982:186317 BIOSIS
DOCUMENT NUMBER: PREV198273046301; BA73:46301
TITLE: CONTROL OF **ADENOVIRUS EARLY** GENE EXPRESSIONS ACCUMULATION OF **VIRAL** MESSENGER RNA AFTER INFECTION OF TRANSFORMED **CELLS**.
AUTHOR(S): PERSSON H [Reprint author]; KATZE M G; PHILIPSON L
CORPORATE SOURCE: DEP MICROBIOL, BIOMED CENT, S-751 23 UPPSALA, SWED
SOURCE: Journal of Virology, (1981) Vol. 40, No. 2, pp. 358-366.
CODEN: JOVIAM. ISSN: 0022-538X.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB Accumulation of **viral** mRNA in the presence of inhibitors of protein synthesis was studied in adenovirus type 5-transformed [**human** embryonic **kidney**] **cell** line (line 293 **cells**). An analysis of the endogenous **viral** mRNA and proteins revealed that only early regions 1A and 1B were expressed in uninfected 293 **cells**. **Viral** mRNA from early regions 2, 3 and 4, and mRNA from early regions 1A and 1B, accumulated in 293 **cells** after infection with adenovirus type 2. **Cells** treated with anisomycin before infection showed a drastic enhancement of mRNA from early region 4 compared with drug-free controls. This increase in **viral** mRNA was **detected** by using filter hybridization, S1 endonuclease mapping and in vitro translation. The rate of transcription of early region 4 nuclear RNA also increased significantly in the presence of anisomycin. The levels of cytoplasmic mRNA from early regions 2 and 3 did not increase in **cells** treated with inhibitors. Multiple **virus** encoded controls appear to operate on the early regions of the adenovirus **genome**.

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ACCESSION NUMBER: 1982:161816 BIOSIS
DOCUMENT NUMBER: PREV198273021800; BA73:21800
TITLE: BIOCHEMICAL STUDIES ON BOVINE ADENOVIRUS TYPE 3 6. IDENTIFICATION OF **VIRUS** SPECIFIC **EARLY PROTEINS** AND TUMOR ANTIGENS.
AUTHOR(S): NIIYAMA Y [Reprint author]
CORPORATE SOURCE: BIOLOGICAL RES LAB, CENTRAL RES DIV, TAKEDA CHEMICAL INDUSTRIES, LTD, OSAKA, JAPAN
SOURCE: Cell Structure and Function, (1981) Vol. 6, No. 2, pp. 133-146.
CODEN: CSFUDY. ISSN: 0386-7196.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB At least 13 species of bovine adenovirus type 3 (BAV3)-specific **early proteins** were **detected** when 2-dimensional electrophoregrams of the BAV3-infected calf **kidney** cells and mock-infected cells were compared. The MW and isoelectric points ranged from 15,000-80,000 and from 5.35-6.85, respectively. Using

an immunoprecipitation method, analyses of T antigens were carried out using 3 types of anti-T sera. The antisera were prepared from tumor-bearing mice as induced by cells transformed with whole or specific fragments of BAV3 **DNA** containing transforming gene(5), and characterized as being BAV3-specific by immunofluorescent studies. Proteins of an apparent MW of 15,000 (15 K [kilodaltons]) and 54 K were identified as common immunoprecipitates between these antisera and extracts of the cells lytically infected with BAV3. Each of these proteins were found among BAV3-specific **early proteins** . The 15 K and 54 K proteins are apparently BAV3 tumor antigens. In the BAV3-transformed cells, a protein with an apparent MW of 80 K instead of 15 K or 54 K protein was **detected** using the same method. Such observations in human adenoviruses have not been reported. The BAV3 15 K protein seems to be suitable for the study of physicochemical properties and functions of T antigen since it can be obtained in large amounts.

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ACCESSION NUMBER: 1979:251054 BIOSIS
DOCUMENT NUMBER: PREV197968053558; BA68:53558
TITLE: NUCLEAR ACCUMULATION OF INFLUENZA **VIRAL** RNA TRANSCRIPTS AND THE EFFECTS OF CYCLO HEXIMIDE ACTINOMYCIN D AND ALPHA AMANITIN.
AUTHOR(S): MARK G E [Reprint author]; TAYLOR J M; BRONI B; KRUG R M
CORPORATE SOURCE: FOX CHASE CANCER CENT, INST CANCER RES, PHILADELPHIA, PA 19111, USA
SOURCE: Journal of Virology, (1979) Vol. 29, No. 2, pp. 744-752. CODEN: JOVIAM. ISSN: 0022-538X.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB **Virus**-specific 32P-labeled complementary (c) **DNA** and 125I-labeled virion RNA were used as hybridization probes to quantitate the number of molecules of cRNA and progeny virion RNA in MDCK [canine **kidney**] **cells** infected with influenza **virus**. The distribution of cRNA between the nucleus and the cytoplasm in cycloheximide-treated **cells** was compared to that found in untreated **cells**, beginning 1 h after infection. A greater percentage of the total cRNA was **detected** in the nucleus of the drug-treated **cells** at all times investigated. For the first 2 h after infection about 50% of the cRNA synthesized in the cycloheximide-treated **cells** was found in the nucleus. These nuclear cRNA molecules were characterized and shown to be polyadenylated transcripts of each of the **genome** virion RNA segments. **Viral** cRNA synthesis was not completely inhibited by the addition of actinomycin D at the beginning of infection, with or without the concomitant addition of cycloheximide. A large fraction (about 90%) of these cRNA sequences were **detected** in the nucleus. Characterization of these nuclear cRNA molecules showed that they contained poly(A) and represented transcripts of those segments coding for proteins synthesized predominantly early after infection (**early proteins**) and those virion RNA segments coding for late proteins. In vitro translation of these cRNA molecules showed that they were functional **virus** mRNA. In contrast to actinomycin D, α-amanitin completely inhibited cRNA synthesis when added at the beginning of infection, and addition of this drug after 1.5 h had no

effect on further cRNA synthesis.

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ACCESSION NUMBER: 1978:245774 BIOSIS
DOCUMENT NUMBER: PREV197866058271; BA66:58271
TITLE: HEAT INACTIVATION OF VACCINIA **VIRUS** PARTICLE ASSOCIATED FUNCTIONS PROPERTIES OF HEATED PARTICLES IN-VIVO AND IN-VITRO.
AUTHOR(S): HARPER J M M [Reprint author]; PARSONAGE M T; PELHAM H R B; DARBY G
CORPORATE SOURCE: DIV VIROL, DEP PATHOL, UNIV CAMB, CAMBRIDGE, ENGL, UK
SOURCE: Journal of Virology, (1978) Vol. 26, No. 3, pp. 646-659. CODEN: JOVIAM. ISSN: 0022-538X.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB The heat inactivation characteristics of several vaccinia **virus** particle-associated functions known to be involved in the transcription of the **genome** were examined. All functions were more resistant to heat than infectivity. Noninfectious particles were generated which exhibited significant levels of activity of all enzymes [**DNA** dependent RNA polymerase, polyadenylate polymerase and RNA methylase] examined, and their properties were investigated both in vitro and in vivo. RNA was synthesized in vitro by such particles, although transport of the RNA into the surrounding medium was defective. This RNA was larger than that made in normal particles but it was polyadenylated and functioned in vitro as a message coding for normal **early proteins**. The sequences transcribed were similar to those transcribed in normal particles, and the production of abnormally large RNA is probably due to a defect in transcriptional termination. No **virus**-specific protein or RNA synthesis in [baby hamster **kidney** PHK **cells**] **cells** exposed to these inactivated particles were **detected** and the loss of infectivity caused by heating is due to a general decline in the activities of a number of particle functions.

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ACCESSION NUMBER: 1979:249140 BIOSIS
DOCUMENT NUMBER: PREV197968051644; BA68:51644
TITLE: COMPARATIVE STUDY BY IMMUNO FLUORESCENCE OF T ANTIGEN AND P ANTIGEN INDUCED BY ADENOVIRUS TYPE 12 IN PERMISSIVE AND NONPERMISSIVE CELLS.
AUTHOR(S): RIBEIRO G [Reprint author]; VASCONCELOS-COSTA J
CORPORATE SOURCE: CENT BIOL, INST GULBENKIAN CIENC, APDO, 14, OEIRAS, PORT
SOURCE: Archives of Virology, (1978) Vol. 58, No. 4, pp. 269-276. CODEN: ARVIDF. ISSN: 0304-8608.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB The development of adenovirus type 12 T antigen and of the complex of antigenic **early proteins** designated as P antigen was studied by immunofluorescence in productively infected KB [**human** oral carcinoma] **cells** and abortively infected RK-13 [rabbit **kidney**] **cells**. T antigen is **detected** in both

cell types very early in infection. In KB cells it presents the well known pattern of nuclear dots and flecks but in RK-13 cells at the time of maximum abundance, 18 h post-infection, T antigen forms a net of long filaments that fills the nucleus. Later, part of the filaments condense into a large aggregate that finally is apparently degraded. P antigen in infected RK-13 cells looks like T antigen in KB cells. In these cells, besides an early phase wherein P antigen is almost indistinguishable from T antigen, a late component is evident under the form of large balls and rosettes. The possible identification of this component with the **DNA** binding protein is discussed.

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ACCESSION NUMBER: 1977:135304 BIOSIS
DOCUMENT NUMBER: PREV197763030168; BA63:30168
TITLE: MULTIPLICATION OF ADENO ASSOCIATED **VIRUS** TYPE 1 IN **CELLS** CO INFECTED WITH A TEMPERATURE SENSITIVE MUTANT OF **HUMAN** ADENOVIRUS TYPE 31.
AUTHOR(S): HANDA H; SHIMOJO H; YAMAGUCHI K
SOURCE: Virology, (1976) Vol. 74, No. 1, pp. 1-15. CODEN: VIRLAX. ISSN: 0042-6822.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: Unavailable

AB A temperature-sensitive mutant (tsA13) of human adenovirus type 31 (H31), defective in **viral DNA** replication, was able to support growth of adeno-associated **virus** type 1 (AAV1) at the nonpermissive temperature (40° C). With the use of this system, the multiplication of AAV1 and AAV1-specific changes were investigated. The latent period of AAV1 growth was shortened by preinfection of cells with H31tsA13 10 h before superinfection with AAV1. The rate of **DNA** synthesis began to rise at about 6 h postinfection (p.i.) with AAV1 and reached its maximum at 16 h p.i. In cells coinfected with H31tsA13 and AAV1, only AAV1 **DNA** was **detected** without the presence of adenovirus **DNA** at 40° C. Replicative intermediates of AAV1 **DNA** were larger than AAV1 **DNA** in neutral and alkaline sucrose gradients. Specific inclusions induced by AAV1 were observed in the nucleus of coinfected and stained cells. Microscopic autoradiogram of coinfected cells revealed that grains (**viral DNA**) were found before the appearance of the inclusions of AAV1 in the interior of the nucleus. The AAV1 virion antigen 1st appeared in the nucleus at about 6 h p.i. with AAV1 and spread into the cytoplasm within 12 h p.i. EM examination of infected cells revealed that the inclusions were aggregates or crystalline arrays of AAV1 particles in the nucleus. Neither adenovirus inclusions nor particles were observed. AAV1 **DNA** replication proceeded in the presence of cycloheximide. The time interval between AAV1 infection and the peak of **DNA** synthesis became shorter, when AAV1 was superinfected at 16 h or later after infection with H31tsA13. AAV1 apparently lacks its own **early protein** and the lack of the **early protein** is complemented by a factor(s) induced in adenovirus-infected **cells**. [**Human** embryonic **kidney** and green monkey **kidney cells** were used.].

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